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Physiologische Indikatoren der körperlichen Leistungsfähigkeit bei Herzinsuffizienz

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Zusammenfassung

Die Steigerung der körperlichen Leistungsfähigkeit scheint neben einer optimierten Pharmakotherapie wesentlich für eine Reduktion der Morbidität bei Patienten mit chronischer Herzinsuffizienz zu sein. Eine Verminderung der körperlichen Leistungsfähigkeit gemessen anhand der spiroergometrisch gemessenen maximalen Sauerstoffaufnahme (Goldstandard) oder der zurückgelegten Distanz im 6-Minuten Gehtest spiegelt meist eine Verschlechterung der klinischen Prognose wider. Jedoch kann man anhand laborgebundener Leistungsuntersuchungen oft nicht das wahre Ausmaß der körperlichen Einschränkungen im Alltag der Patienten messen. Die körperliche Belastbarkeit im Alltag ist aber hinsichtlich des Wohlbefindens des Patienten ausschlaggebend und wird zur Einteilung des Schweregrades der Herzinsuffizienz nach New York Heart Association (NYHA) herangezogen.

In der vorliegenden Arbeit werden verschiedene Methoden zur Erfassung der Alltagsaktivität und Leistungsfähigkeit unter Alltagsbedingungen bei Patienten mit chronischer Herzinsuffizienz untersucht und miteinander verglichen. Zudem wird evaluiert, ob die mittels Accelerometer objektiv gemessene Alltagsaktivität sich als Maß der körperlichen Leistungsfähigkeit eignet und somit Rückschlüsse auf die ergometrisch gemessene maximale Leistungsfähigkeit (VO_{2peak}) und die Gehstrecke im 6-Minuten Gehtest (6MWT) erlaubt. Ziel dieser Arbeit ist es, die Erfassung und Quantifizierung der körperlichen Alltagsaktivität zu optimieren, um diese in die Risikobewertung der Herzinsuffizienz mit einfließen lassen zu können.

Um dies umzusetzen, wurden wesentliche physiologische Indikatoren der körperlichen Leistungsfähigkeit bei Patienten mit Herzinsuffizienz gemessen und deren Zusammenhänge zueinander herausgearbeitet. Es bestehen physiologisch sinnvolle Beziehungen zwischen der Gehstrecke im 6MWT, der VO_{2peak} bei der Fahrradergometrie, der mittels Accelerometer erfassten Schrittzahl und der Alltagsaktivität. Im 6MWT zeigt die Schrittzahl eine signifikante Korrelation mit der zurückgelegten Gehstrecke (m) und kann im klinisch relevanten Leistungsbereich des 6-Minuten Gehtests (unterhalb einer

Gehstrecke von 350m/6min) als diskriminierend zwischen den klinischen Herzinsuffizienz-Schweregraden NYHA II und III angesehen werden. Somit kann die im 6-Minuten Gehtest zurückgelegte Schrittzahl als telemedizinisch erfassbarer Parameter zur Beurteilung der Leistungsfähigkeit in Betracht gezogen werden.

Auch die Alltagsaktivität gemessen anhand der täglichen Gehzeit (Minuten) zeigt eine enge Beziehung sowohl zur ergometrisch ermittelten VO_{2peak} als auch zur zurückgelegten Distanz im 6-Minuten Gehtest. Unter den Parametern, die die Alltagsaktivität widerspiegeln, zeigte sich vor allem die Gehintensität (Aktivitätsgruppen *Walk* und *Fast Walk*) als wesentlich, um den NYHA III Schweregrad von NYHA I und NYHA II zu unterscheiden. Für die Diskriminierung des NYHA-III Schweregrades ist der Parameter *Fast Walk* (Minuten/Tag) der ergometrisch ermittelten VO_{2peak} in ihrer Diskriminationsfähigkeit gleichwertig. Daraus lässt sich schlussfolgern, dass sich sowohl die im 6MWT zurückgelegte Schrittzahl als auch die Alltagsaktivität als telemedizinisch erfassbare Parameter zur Beurteilung der Leistungsfähigkeit bei Patienten mit chronischer Herzinsuffizienz eignen.

Summary

In recent years it has been shown that improved exercise capacity along with the advent of new medication is essential for the reduction of morbidity and mortality in patients with chronic heart failure. A decrease in exercise capacity measured by means of maximal oxygen consumption (VO_{2peak}) or distance walked in the 6-minute walk test (in metres) typically indicates a worsening in clinical prognosis. Nevertheless, laboratory based exercise testing is not always an accurate reflection of a patient's true functional limitation in everyday life. Exercise capacity associated with daily living is however indicative of a patient's actual well being and is an important determinant in judging the severity of heart failure according to the New York Heart Association (NYHA).

In this thesis, different methods for measuring daily activity in patients with heart failure were investigated and compared to one another. Moreover, it was evaluated if objective measures of everyday physical activity by means of accelerometer can be used as a measure of overall exercise capacity, in particular VO_{2peak}. The goal was to optimize methods of physical activity measures, so that these can be incorporated into clinical prognosis.

In order to accomplish this, relevant physiological indicators of exercise capacity in patients with chronic heart failure were evaluated and put in context to each other. There are physiologically useful associations between distance walked in the 6-minute walk test (6MWT), VO_2peak measured by means of cycle ergometry, step count and daily activity levels measured by means of accelerometry. In the 6MWT, there is a significant correlation of overall step count with total distance walked (metres). Moreover, in the clinically relevant cut off range of the 6MWT (i.e. 300m/6 min), step count was able to discriminate patients in terms of worsening cardiovascular capacity. Therefore, 6MWT step count can be considered as a useful indicator of exercise capacity in patients with heart failure.

Daily activity levels measured by means of total daily walking time (minutes/day) also showed a strong association with maximal and functional indicators of exercise capacity (VO_{2peak} and 6MWT distance, respectively). Particularly, walking intensity (activity modes *walk* versus *fast walk*) was decisive in discriminating NYHA III patients from NYHA I and II patients. The parameter *fast walk* showed the highest accuracy of prediction along with VO_{2peak} in identifying patients with severe heart failure (NYHA III). In conclusion, both the 6MWT step count as well as daily activity levels seem suitable for evaluating exercise capacity in patients with chronic heart failure and can be considered in telemedical patient monitoring.

Abkürzungsverzeichnis

ACT = Active time

AHA = American Heart Association

APM = Aipermon Accelerometer

AT = Anaerobic threshold

AUC = Area under the curve

CHF = Chronic heart failure

CPET = Cardiopulmonary exercises test

DCM = Dilated cardiomyopathy

DHC = Digital hand counter

FWLK = Fast walk

GET = Graded exercise test

HFPEF = heart failure with preserved ejection fraction

HFREF = heat failure with reduced ejection fraction

ICM = Ischemic cardiomyopathy

LVEF = Left ventricular ejection fraction

NYHA = Ney York Heart Association

PAS = Passive

RER = Respiratory exchange ratio

ROC = Receiver operating characteristics

TWT = Total walking time

6MWT = Six minute walk test

VE = Ventilation

VMU = Vector Magnitude Unit

VO_2peak = Peak oxygen uptake

WLK = Walk

Inhaltsverzeichnis

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1 Einleitung

Das Projekt „Partnership for the Heart“ ist eine randomisierte, offene, multizentrische, kontrollierte Studie zur Evaluation der Mortalität und Morbidität bei Patienten mit chronischer Herzinsuffizienz. So soll verglichen werden, in wieweit ein telemedizinisches Therapiemanagement einer Standardtherapie hinsichtlich Sterblichkeit, Hospitalisierungsrate und Wirtschaftlichkeit überlegen ist. Ein wesentlicher Aspekt der telemetrischen Überwachung ist die Erfassung und Quantifizierung der körperlichen Aktivität. Dieser Parameter hat sich innerhalb der letzten Jahre neben einer optimierten Pharmakotherapie als wesentlich für eine Reduktion der Krankenhauseinweisung bei Patienten mit chronischer Herzinsuffizienz gezeigt (1;2). Eine Verminderung der körperlichen Leistungsfähigkeit gemessen anhand der maximalen Sauerstoffaufnahme mittels Spiroergometrie (Goldstandard), der hinterlegten Distanz im 6-Minuten Gehtest, oder mittels Quantifizierung der körperlichen Alltagsaktivität, spiegelt meist eine Verschlechterung der klinischen Prognose wider (3). Jedoch kann man anhand laborspezifischer Leistungsuntersuchungen oft nicht das wahre Ausmaß körperlicher Einschränkungen im Alltag der Patienten messen. Ziel dieser Arbeit ist es somit, die Erfassung und Quantifizierung der körperlichen Alltagsaktivität zu optimieren, um diese in die Risikobewertung der Prognose mit einfließen lassen zu können.

Um die körperliche Alltagsaktivität von Patienten mit Herzinsuffizienz genau messen und dokumentieren zu können, wurde von der Firma Aipermon® ein Aktivitätsmessgerät entwickelt (APM), welches über einen drei dimensionalen Beschleunigungsmesser ein Bewegungsprofil über einen längeren Zeitraum erfassen und für eine statistische Auswertung speichern kann (4). Allerdings muss dieses Gerät hinsichtlich seiner Messgenauigkeit bei einem primär geringen und langsamen Aktivitätsprofil evaluiert werden, damit es für die telemedizinische Nutzung bei Patienten mit chronischer Herzinsuffizienz eingesetzt werden kann. Hierzu bedarf es verschiedener klinischer Tauglichkeitsstudien, die im Vorfeld durchgeführt werden müssen.

Das Thema dieser Arbeit bezieht sich auf die Evaluation des APM Aktivitätssensors, mit dessen Hilfe die Alltagsaktivität und gezielte Aktivität von Patienten mit Herzinsuffizienz quantifiziert und dokumentiert werden soll. Das telemetrische Aktivitätsmonitoring soll dazu dienen eine Verschlechterung des Schweregrad der Herzinsuffizienz rechtzeitig erkennen zu können und somit als Entscheidungshilfe für die Vorstellung beim Hausarzt bzw. für die Klinikeinweisung zu dienen. Die Ergebnisse dieser Arbeit fließen in die Gesamtauswertung der telemetrischen Studie „Partnership for the Heart (BMBF NCT 00543881) mit ein.

2 Hintergrund

2.1 Prävalenz und Inzidenz der Herzinsuffizienz

Die Herzinsuffizienz ist eine der häufigsten, internistischen Erkrankungen und Schätzungen zufolge leiden in Nordamerika und Europa mehr als 15 Millionen Menschen an dieser Krankheit. Jährlich kommen ca. 1,5 Millionen neue Fälle hinzu (5;6). Prävalenz und Inzidenz der Herzinsuffizienz sind altersabhängig. Im Alter von 45 bis 55 Jahren leiden weniger als 1 Prozent der Bevölkerung an Herzinsuffizienz, 65- bis 75-Jährige bereits zu 5 Prozent und über 80-Jährige zu fast 10 Prozent. Männer sind etwa 1,5-fach häufiger betroffen als gleichaltrige Frauen (7). In der Todesursachenstatistik Deutschlands liegt die Herzinsuffizienz auf Platz drei noch vor Krebserkrankungen wie Brust-, Lungen- oder Darmkrebs. Bei Frauen rückt die Herzinsuffizienz mit einem Anteil von 7,4 % unter den häufigsten Todesursachen sogar an die zweite Stelle vor (8;9)

2.2 Krankheitsbild der Herzinsuffizienz

Bei 80–90 Prozent der Erkrankten liegt eine Funktionsstörung des Herzmuskels im Sinne einer Herzmuskelschwäche vor und ist definitionsgemäß das *„Unvermögen des Herzens die vom Körper benötigte Sauerstoffversorgung der metabolisch aktiven Gewebe zu gewährleisten“* (10;11). Die häufigsten Ursachen der Herzinsuffizienz in den westlichen Ländern sind die koronare Herzkrankheit und die arterielle Hypertonie (12;13). Weitere Ursachen umfassen unter anderem primäre Herzmuskel-

erkrankungen, Koronaratherosklerosen, Herzklappenerkrankungen, rheumatische Erkrankungen welche die Myokardfunktion beeinträchtigen, und eine chronisch konstriktive Perikarditis (Myokarditis), durch welche der Herzmuskel möglicherweise entzündlich infiltriert wird (14). Als Folge dessen kommt es zu einer eingeschränkten Kontraktionsfähigkeit und somit Pumpfunktion (EF%) des Myokards, die wiederum zu einer Verminderung der systemischen und peripheren Durchblutung führen (11). Die Herzinsuffizienz besitzt eine differenzierte Symptomatik mit Dyspnoe und eingeschränkter Belastbarkeit als den beiden Leitsymptomen. Weitere typische Beschwerden sind die Orthopnoe, vorschnelle Ermüdbarkeit, zerebrale Symptome, periphere Ödeme, Venenstauungen, akute oder chronische Vergrößerungen von Leber und Milz (Hepato- und Splenomegalie), sowie eine krankhafte Ansammlung von Flüssigkeit in der freien Bauchhöhle (Aszites) (15).

Für den klinischen Krankheitsverlauf wird die Herzinsuffizienz folgender maßen differenziert: Linksherz-, Rechtsherz- oder Globalinsuffizienz, Ruhe- oder Belastungsinsuffizienz, diastolische oder systolische Herzinsuffizienz, kompensierte oder dekompensierte Herzinsuffizienz, akuter oder chronischer Verlauf. Die Einteilung der Ausprägung des Krankheitsbildes erfolgt nach den ABCD-Stadien der American Heart Association (AHA) oder nach den Stadien der New York Heart Association (NYHA), welche primär auf den Kriterien der subjektiven Belastbarkeit des Patienten basieren. Nach zuletzt genannter NYHA-Einteilung wird die Herzinsuffizienz in 4 Stadien eingeteilt (NYHA I – IV), wobei Personen in Stadium I sowohl in Ruhe als auch unter Belastung noch beschwerdefrei sind. Sobald Beschwerden in Ruhe auftreten, spricht man von einem NYHA-Stadium IV (16).

Die therapeutischen Maßnahmen bestehen vorwiegend aus der Pharmakotherapie die sich heute aus ACE-Hemmer, Diuretika, Digitalis-Präparate, vasodilatatorische Vor- und Nachlastsenker, ß-Blocker, positiv inotrope Substanzen und Phosphodiesterasehemmer zusammensetzt. Aber auch die Lebensstiländerung, sowie Gewichtskontrolle und körperliche Bewegung stellen weitere wichtige Therapieelemente dar (17;18).

2.3 Die klinische Prognose der Herzinsuffizienz

Die pathophysiologischen Veränderungen der Herzinsuffizienz führen mit der Verminderung der körperlichen Leistungsfähigkeit als Folge zu einer ungünstigen klinischen Prognose (19). Als Entscheidungshilfe für die kardiale Prognose wird die spiroergometrisch ermittelte maximale Sauerstoffaufnahme (VO_2peak) herangezogen. Auch der im 6-Minuten Gehtest (6MWT) hinterlegten Distanz (m) wird bei der Beurteilung der klinischen Prognose ein aussagekräftiger Stellenwert beigemessen. Deutliche Verschlechterungen dieser Parameter gehen mit einer erhöhten Morbidität und Mortalität der Patienten einher (20-23). Allerdings werden beide Leistungsuntersuchungen hinsichtlich ihrer Aussagekraft über die Mortalität unterschiedlich beurteilt. Für die Kurzzeitprognose (6 Monate) wird die Distanz (m) im 6MWT, für die Mittel- und Langzeitprognose die VO_2peak als günstiger angesehen (24;25). In der multivariaten Analyse wird der VO_2peak der höhere prädikative Stellenwert beigemessen (26). Die testspezifische maximale Sauerstoffaufnahme (VO_2peak) wird auch als Indikation einer Herztransplantation in Betracht gezogen (27).

2.4 Herzinsuffizienz und Bewegung

Während es im letzten Jahrzehnt noch galt körperliche Aktivität bei Herzinsuffizienz möglichst zu vermeiden (28), ist es heute ein wichtiger Bestandteil der Therapie geworden (5;29;30). Anhand zahlreicher Studien konnte gezeigt werden, dass körperliche Bewegung in der Therapie neben einer optimierten Pharmakotherapie zu einer signifikanten Verminderung in der Krankenhauseinweisung der Patienten mit chronischer Herzinsuffizienz führt (31;32). Zudem konnte durch regelmäßige körperliche Aktivität eine Verbesserung subjektiver und objektiver Parameter der Belastbarkeit und Leistungsfähigkeit der Patienten erzielt werden (33-36). Dies spiegelt sich nicht nur in einer Verbesserung der maximallen Sauerstoffaufnahme (VO_2peak) und der im 6-Minuten Gehtest hinterlegten Distanz (m) wieder, sondern auch in einer verbesserten Lebensqualität und gesteigerten Alltagsaktivität der Patienten (37;38).

2.5 Die Rolle der Bewegungserfassung in der Therapie

Obwohl testspezifische physiologische Leistungsparameter, wie z.B. die maximale Sauerstoffaufnahme (VO_2peak) oder die im 6-Minuten Gehtest hinterlege Distanz, optimale Rückschlüsse auf die körperliche Leistungsfähigkeit liefern, stellen sie nicht immer praktikable Meßmethoden dar (39). Besonders die Quantifizierung der körperlichen Alltagsaktivität ist dadurch nicht möglich.

Bei Patienten mit Herzinsuffizienz spielt die Alltagsbewegung und somit die kontinuierliche Kontrolle der körperlichen Belastbarkeit eine wichtige Rolle, da diese Rückschlüsse auf den eigentlichen Gesundheitszustand erlaubt (40;41). Die Erhebung und Quantifizierung der körperlicher Alltagsaktivität ist somit ein wichtiger Bestandteil der Therapie und ermöglicht es, Morbiditäts- und Mortalitätsentwicklungen in einen direkten Bezug zur körperlichen Aktivität zu stellen (3). Um jedoch eine aussagekräftige Beziehung zwischen körperlicher Bewegung, Therapie und Prognose herstellen zu können und um leitliniengerechte Empfehlungen zur körperlichen Aktivität zu etablieren, ist eine exakte Erfassung des Bewegungsprofils erforderlich.

Deshalb bedarf es zusätzlicher Meßmethoden, welche die körperliche Aktivität möglichst unabhängig von jeglichen Einflussfaktoren objektiv erfassen können. In dieser Arbeit werden verschiedene Methoden zur Aktivitätserfassung hinsichtlich ihrer Tauglichkeit bei Patienten mit Herzinsuffizienz untersucht. Im Vordergrund steht der dreidimensionale Aktivitätssensor der Firma Aipermon®. Die Anforderungen an den Aktivitätssensor beziehen sich primär auf die genaue Bewegungserkennung und Quantifizierung von langsamen Gehgeschwindigkeiten bei Patienten mit chronischer Herzinsuffizienz.

2.6 Bisherige Methoden der körperlichen Aktivitätserfassung

Verschiedene Methoden wurden bisher zur Erfassung der körperlichen Alltagsaktivität bei Patienten mit Herzinsuffizienz eingesetzt. Diese sind unter anderem die Fragebogenerhebung, Pedometer oder Schrittzähler und Accelerometer wie z. B. Aipermon oder RT3. Diese Methoden haben

unterschiedliche Vor- und Nachteile, die im nachfolgenden Teil kurz diskutiert werden.

2.6.1 Fragebogen

Die Anwendung von Aktivitätsfragebögen ist eine einfache und kostengünstige Methode der Aktivitätserfassung und kann vom Patienten selbst verabreicht, per Post, oder per Telefoninterview erhoben werden. Mittels Fragebögen kann ein weites Spektrum an verschieden Aktivitäten erfasst werden. Allerdings ist hier keine objektive Datenerhebung möglich, sondern nur eine subjektive Datenerhebung die von der Wahrnehmung des Patienten abhängt. Diese wird in vielen Fällen durch gesellschaftliche Norm/Sollwerte beeinflusst und entspricht somit nicht immer dem eigentlichem Aktivitätsniveau des Befragten (42-46). Somit werden Aktivitäten mit hoher Intensität wie z.B. gezielter Sport oft überschätzt, wohingegen Aktivitäten mit generell niedrigen Intensitäten wie z.B. Gehen im Alltag vergessen und somit unterschätzt werden (47). Zudem umfasst die Datenerfassung meist einen längeren Zeitraum (Woche/Monat). Dies kann bei Patienten mit eingeschränktem Erinnerungsvermögen, ins besondere bei älteren Menschen, das Gedächtnis überfordern und somit die exakte Datenerhebung stark beeinflussen (48-50).

Ein weiterer Nachteil der Aktivitätserfassung mittels Fragebogen ist, dass sich die Fragen vorwiegend auf gezielten Sport oder Transport beziehen, welche sich meistens durch ihre höheren Bewegungsintensitäten auszeichnen (z.B. Laufen, Schwimmen, Radfahren etc.). Auch die Zeiträume der erfragten Bewegungsabschnitte sind relativ hoch angesetzt (15/30/60min) (44;51). Bewegungen mit geringer Intensität wie z. B. Hausarbeit, willkürliche Fußgänge oder Stehen, werden entweder nur gering oder gar nicht berücksichtigt (52). Somit ist die mittels Fragebogen mögliche Aktivitätserfassung für Patienten mit einem stark eingeschränktem Leistungsniveau (NYHA III) zu intensiv und eignet sich nur bedingt zur Ermittlung der Alltagsaktivität (40;41;53).

Zudem ist mittels Fragebogen kein engmaschiges Monitoring auf Tagesbasis möglich. Gerade die Stadien NYHA II und III bedürfen jedoch einer präzisen Methode zur Erfassung ihres Aktivitätsniveaus, da davon die Vorstellung beim

Arzt oder die Klinikaufnahme abhängen soll. Dennoch scheint es sinnvoll, die nicht geräteabhängige Methode der Fragebogenerhebung mit dem APM Accelerometer zu vergleichen. Hierzu wurde der für Herzpatienten validierte „Lüdenscheider Aktivitätsfragebogen“ herangezogen (51).

2.6.2 Pedometer

Pedometer sind eine weitere kostengünstige und relativ einfach zu handhabende Methode der Aktivitätserfassung und finden in zahlreichen Interventionsstudien ihre Anwendung. Sie sind kleine batteriegesteuerte elektronische Geräte, die an der Hüfte befestigt werden und das Aktivitätsmaß nach geleisteter Schrittzahl anhand eines Federpendels quantifizieren. Ursprünglich wurde das Pedometer von japanischen Walking Clubs eingesetzt und als „10 000 steps meters“ (japanisch: *manpo-kei*) bezeichnet (54). In 1983 beschrieb Hatano (55) das 10 000 Schritte einer zusätzlichen Energieverbrennung von 300 kcal entsprechen. Dieser Mehrumsatz wurde von Dr. Ralph Pfaffenberger in der „College Alumnus Health Study“ als erforderlich beschrieben, um das erstmalige Herzinfarktrisiko zu senken (56). Basierend auf diesen Ergebnissen wurde das Aktivitätsniveau an hand der Schrittzahl folgender maßen festgelegt:

Aktivitätsniveau	**Schritte pro Tag**
Inaktiv	<5000
Wenig Aktiv	5000-7499
Ausreichend Aktiv	7500-9999
Aktiv	10000-12499
Sehr Aktiv	>12500

Tabelle 1. Aktivitätsniveau gemessen anhand der mit Pedometer ermittelten täglichen Schrittzahl; adaptiert nach Tudor-Locke und Bassett (57).

In einer Übersichtsarbeit von Bravata et al., in der acht randomisierte Kontrollstudien und 18 Observationsstudien untersucht wurden, konnte gezeigt werden, dass Pedometer zusätzlich als Motivationshilfe dienen (58). Die körperliche Aktivität der Beteiligten konnte durch die Anwendung eines Pedometers im Durchschnitt um ca. 2200-25000 Schritte pro Tag gesteigert werden. Weitere zusätzliche Schritte spiegelten sich in einer positiven

Senkung des Body Mass Index (BMI) und des Blutdrucks wieder. Zudem konnte Walsh et al. anhand eines Pedometers zeigen, dass die Prognose bei Patienten mit Herzinsuffizienz bei einer Schrittzahl von weniger als 25.000 Schritte/Woche deutlich schlechter liegt als bei denjenigen oberhalb dieses Limits (3).

Es gibt eine Anzahl erhältlicher Pedometer die sich stark hinsichtlich ihrer Messgenauigkeit unterscheiden. Besonders bei niedrigen Geschwindigkeiten (< 40 m/min) und einer unregelmäßigen Gehbewegung unterschätzen sie meist die geleistete Schrittzahl und erscheinen deshalb für ältere Herzpatienten mit starken funktionellen Einschränkungen weniger geeignet (59-62). Diese erreichen im 6-Minuten Gehtest häufig Gehstrecken unter oder um die 300 Meter, legen also in Durchschnitt um die 50 m/min zurück. Aus diesem Grund scheint das Pedometer zur Erfassung der Alltagsaktivität in älteren Patienten mit Herzinsuffizienz weniger geeignet und findet seine Anwendbarkeit eher in gesunden Probanden mit normalen Aktivitätsprofil (57;63-65). Dennoch sollte das Pedometer in einem kontrollierten Setting zusammen mit den nachfolgend diskutierten Accelerometern getestet werden. Hierzu wurde das Omron HJ-720ITC Pedometer herangezogen und untersucht.

2.6.3 Aktivitätssensoren

Accelerometer sind ebenfalls batteriebetriebene elektronische Bewegungssensoren, die an der Hüfte getragen werden. Sie messen mittels spezifischer Sensoren (Fühler) die Beschleunigung einer Bewegung, indem die auf eine Testmasse wirkende Trägheitskraft bestimmt wird. Somit kann z. B. bestimmt werden, ob eine Geschwindigkeitszunahme oder -abnahme stattfindet, um somit die Intensität der Bewegung zu erfassen. Die Bewegungsbeschleunigungen werden vorwiegend in der vertikalen Ebene gemessen, wie z.B. der eindimensionale ActiGraph (Fort Walton Beach, Florida, USA). Allerdings gibt es auch dreidimensionale Accelerometer, die Beschleunigungen sowohl in der vertikalen (y-Achse), horizontalen (x-Achse) und diagonalen (z-Achse) Ebene bestimmen können, wie z.B. der RT3 (Stay Healthy, USA) oder der APM (Aipermon® GmbH Germany). Dadurch kann ein detailliertes Bewegungsprofil erstellt werden.

Accelerometer vereinigen Schrittzähler und Bewegungssensor in einem Gerät und geben Aktivität meistens in Form von *Activity Counts* wieder. Diese steigen linear zur Bewegungsintensität an. Obwohl mittels Accelerometer vorwiegend nur Gehbewegungen erfasst werden können, erlaubt diese Methode eine objektive Datenerfassung der willkürlichen Alltagsaktivität. Diese umfasst in Patienten mit eingeschränkter Leistungsfähigkeit oft den Hauptanteil an körperlicher Bewegung (41;66-68). Accelerometer korrelieren detaillierte Bewegungsinformationen mit dem dazu gehörigem Tageszeitpunkt und können sowohl Gehintensitäten als auch Schritte bei langsamen Gehbewegungen exakt unterscheiden (69-72). Ein Nachteil von Accelerometern ist jedoch der relativ hohe Kostenaufwand (≥ 300 €) und die nötigen technischen Vorraussetzungen, welche die Praktikabilität der Geräte für den Alltagsgebrauch in Frage stellen.

In dieser Studie wird der RT3 und der APM im Detail untersucht. Der RT3 ist ein bereits validiertes Gerät (73;74), jedoch aufgrund seiner vorgegebenen Frequenzgrenzen in der Differenzierung zwischen moderater und niedriger Intensität limitiert (75), was den Einsatz bei Herzinsuffizienz-Patienten einschränkt. Nach 14 Tagen Nutzung im Langzeitversuch haben 20% der Studienteilnehmer den RT3 nicht mehr getragen was das Gerät hinsichtlich der Compliance in Frage stellt (76). Für den telemetrischen Einsatz bei Patienten mit Herzinsuffizienz kommt bisher nur der APM der Firma Aipermon® in Frage und wird somit hinsichtlich seiner Tauglichkeit untersucht. Jedoch ist es sinnvoll den APM mit einem bereits etablierten Gerät zu vergleichen.

3 Studienziele

Die Inhalte dieser Arbeit beziehen sich auf folgende Studienziele:

3.1 Evaluation des APM Aktivitätssensors hinsichtlich seiner Messgenauigkeit, mit dessen Hilfe die Alltagsaktivität und gezielte Aktivität von Patienten mit Herzinsuffizienz quantifiziert und dokumentiert werden soll.

3.2 Differenzierung verschiedener Aktivitätsparameter gemessen mit dem APM, RT3 und dem Omron Pedometer und deren Eignung den NYHA Schweregrad der Herzinsuffizienz zu unterscheiden.

3.3 Nützlichkeit der Alltagsaktivität als Indikator für den klinischen Krankheitsverlauf und als Entscheidungshilfe für die Klinikeinweisung im Vergleich zu etablierten Leistungsparametern (6 MWT, VO_2peak).

3.4 Verbesserung der telemetrischen Überwachung von Patienten mit Herzinsuffizienz durch den Einsatz des Aktivitätssensors.

4 Spezifische Fragestellungen

Folgende Untersuchungen wurden angestrebt um die spezifischen Fragestellungen zu beantworten:

4.1. Vergleich der mittels Pedometer gemessenen Schrittzahl mit der mittels APM gemessenen Schrittzahl bei definierten Geschwindigkeiten auf dem Laufband-ergometer und im Feldtest., insbesondere bei niedrigen Gehgeschwindigkeiten (≥ 20m/min).

4.2. Korrelation zwischen der Gehstrecke im 6-Minuten Gehtest, den Aktivitätsparametern des APM, Pedometers (Schrittzahl) und des RT3 (Vektormagnitude), und der VO_2peak der Fahrradergometrie.

4.3. Messung der Alltagsaktivität mittels APM und Pedometer über 7 Tage im Vergleich zu der Fragebogenerfassung.

4.4. Untersuchung der respiratorischen Belastungsparameter während des 6-Minuten Gehtests gemessen mittels einer mobilen Spiroergometrie. Korrelation zwischen der VO_2peak im 6MWT und der VO_2peak der Fahrradergometrie in Bezug zum Schweregrad der Herzinsuffizienz.

5 Studienpopulation

Für die Klärung der im Studienprotokoll vorgesehenen Teilstudien wurden 50 Patienten mit Herzinsuffizienz untersucht. Die Probanden wurden mit Hilfe eines Zeitungsinserats und durch die Mithilfe der Herzinsuffizienzambulanz des Universitätsklinikums rekrutiert. Einschlusskriterien waren chronische Herzinsuffizienz definiert nach New York Heart Association (NYHA) Klasse I – III, unabhängig von Alter, Geschlecht und Krankheitsgeschichte. Ausschlusskriterien waren medizinisch unstabile Krankheitsbefunde in denen körperliche Belastung kontraindiziert war, oder wenn der Patient nicht ohne Hilfe Gehen konnten. Die Studie wurde von der diesigen Ethikkommission genehmigt und entsprach den Bedingungen gemäß der Deklaration von Helsinki. Alle Patienten unterschrieben eine schriftliche Einwilligungserklärung. Folgende Untersuchungen wurden von dem zuständigen Prüfarzt bei jedem einzelnen Patienten durchgeführt: Anamnese, körperliche Untersuchung, Anthropometrie, Echokardiographie, Ruhe EKG, Labor, Spiroergometrie auf dem Fahrrad und ein 6-Minuten Gehtest. Die Leistungsuntersuchungen wurden randomisiert durchgeführt. Anhand der klinischen Daten wurde jeder Patient wiederholt von zwei unabhängigen Ärzten in die jeweiligen NYHA Klassen eingeteilt. Somit entstand eine Patientenklassifizierung von N = 12 NYHA I, N = 19 NYHA II und N = 19 NYHA III. Eine detaillierte Charakterisierung des untersuchten Studienkollektivs ist in Tabelle 2 und den einzelnen Publikationen zu finden.

6 Untersuchungen

6.1 Fahrradergometrie

Jeder Patient absolvierte eine Spiroergometrie auf dem Fahrradergometer (Sport Excalibur, Lode Medical Technology, Niederlande). Guidelines gemäß (77) wurde ein Rampenprotokoll gewählt (Start bei 10 Watt, Steigerung um 10 Watt pro Minute). Die Patienten wurden aufgefordert sich bis zur subjektiven Erschöpfung zu belasten (Borg ≥ 18), oder bis schwerwiegende kardiale Arrhythmien auftraten. Respiratorische Atemgase wurden mit Hilfe des ZAN Metabolic Cart gemessen. (ZAN 600 USB CPX, nSpire Health GmbH, Germany). Herzfrequenz wurde anhand eines 12-Kanal EKGs kontrolliert,

Borgskala wurde jede Minute notiert und Blutdruck wurde manuell am Ende jeder Belastungsminute sowohl als auch nach jeder zweiten Erholungsminute gemessen. Nach der Belastung folgten fünf Minuten aktive Erholung. Hier wurden die Patienten aufgefordert bei geringem Widerstand die Beine in Bewegung zu halten um Blutstauungen in den Extremitäten zu vermeiden.

6.2 Laufband und Feldtest bei definierten Geschwindigkeiten

Um den APM (Meddlogger, Aipermon® GmbH, Germany) hinsichtlich seiner Meßgenauigkeit bei unterschiedlichen Gehgeschwindigkeiten zu untersuchen, wurde die mit APM und Pedometer (OMRON, HJ-720ITC Walking style Pro) gemessene Schrittzahl mit der mittels digitalen Handzähler (HC-1, Voltcraft, Hirschau, Germany) gemessenen Schritte bei definierten Geschwindigkeiten auf dem Laufband und im Feldtest verglichen. Die Patienten wurden aufgefordert, jeweils sechs Minuten bei jeder Geschwindigkeit (40, 50, 60, 70 und 80 m/min) auf dem Laufband und im Freien zu gehen. Im Feldtest wurde die Gehgeschwindigkeit anhand einer Signaluhr vorgegeben. Das Pedometer wurde an der rechten Hüfte und das Accelerometer an der linken Hüfte befestigt. Das Laufband (HP Cosmos pulsar 4.0) wurde vor jeder Untersuchung kalibriert. Die Abweichungen zwischen den ausgewählten Geschwindigkeitsstufen lag bei ± 5%.

6.3 6-Minuten Gehtest

Die Patienten absolvierten den 6-Minuten Gehtest (6MWT) auf einem abgemessenen Pendelparcours über 40 m Länge. Der Parcours wurde alle 5 m mit einer Pylone markiert. Der APM (Meddlogger, Aipermon® GmbH, Germany) wurde wie in den anderen Untersuchungen an der linken Hüfte, der RT3 (Stay Healthy, USA) und das Omron-Pedometer (OMRON, HJ-720ITC Walking style Pro) an der rechten Hüfte getragen. Die zurückgelegte Schrittzahl wurde mit einem digitalen Handzähler (HC-1, Voltcraft, Hirschau, Germany) kontrolliert und jede Minute notiert um den Schrittzahlverlauf über 6 Minuten nachvollziehen zu können. Gleichzeitig wurde auch die zurückgelegte Strecke pro Minute notiert.

Um die respiratorischen Atemgase während des 6MWT bestimmen zu können wurden die Patienten zusätzlich aufgefordert einen 2.5 kg schweren Rucksack

anzulegen in dem eine mobile Spirometrie eingebaut war (ZAN600 Mobile, nSpire Health GmbH, Oberthulba, Germany). Das Gerät wurde vor jeder Belastung erneut kalibriert und die Atemgase wurden in 10 Sekunden Intervalle gemessen. Die Messungen der Atemgase wurden anhand einer Radioantenne zu einer Basisstation gesendet und die Daten anschließend mit einer dafür konzipierten Software (ZAN WINGPI 3.00) veranschaulicht und ausgewertet.

6.4 Langzeituntersuchung der Alltagsaktivität (7 Tage)

Für den Langzeittest wurden die Probanden aufgefordert, den APM und das Omron Pedometer eine Woche zu tragen (zum Beispiel Mittwoch bis Mittwoch). Am ersten Tag bekamen die Probanden die Geräte ausgehändigt und brachten sie am achten Tag zurück. Der erste und letzte Tag waren keine vollen Tage und entsprachen nicht dem üblichen Alltagsablauf der Patienten. Diese unvollständigen Tage wurden von der Auswertung des Langzeitaktivitätsmaßes ausgeschlossen. Es wurden also 6 volle Tage ausgewertet. Die Patienten wurden gebeten, den APM nur beim Baden, Duschen und Schlafen abzulegen. Die aktive Tragezeit des APM betrug damit täglich durchschnittlich 13,02 Stunden für NYHA I, 12,75 Stunden für NYHA II und 12,51 Stunden für NYHA III. Nach Aussage der Patienten wurde das Pedometer gemeinsam mit dem Accelerometer an- und abgelegt.

6.5 Aktivitätsfragebogen

Jeder Patient wurde gebeten einen validierten Fragebogen reflektierend ihrer Alltagsaktivität auszufüllen (51). Mit dem "Lüdenscheider Aktivitätsfragebogen“ wird überprüft, ob der "wöchentliche Energiemehrumsatz durch körperliche Aktivität und Sport" die durch eine Reihe von wissenschaftlichen Studien belegte gesundheitlich präventiv wirksame 2000 Kcal-Schwelle pro Woche erreicht. Werden 2000 Kcal pro Woche überschritten (entspricht einer Gesamtpunktzahl von ≥ 40 Punkten), hat man ein hohes Aktivitätsniveau mit einer „hoch wirksamen“ Gesundheitsprävention durch Sport. Liegt der Energiemehrumsatz (EMU) 1000 < EMU ≤ 2000 Kcal pro Woche (entsprechend einer Gesamtpunktzahl von ≥ 30 - < 40 Punkten), so hat man ein für die Gesundheitsprävention „ausreichendes“ Aktivitätsniveau. Bei 500 < EMU ≤ 1000 Kcal pro Woche (entsprechend einer Gesamtpunktzahl von ≥ 15

und < 30 Punkten), erfüllt man „gerade noch“ die Mindestanforderungen an körperlicher Aktivität pro Woche und liegt der EMU ≤ 500 Kcal pro Woche (entsprechend einer Gesamtpunktzahl von ≤ 14 Punkten), ist man „zu wenig aktiv“ und zahlreichen Risikofaktoren durch Bewegungsmangel ausgesetzt.

7 Statistische Methoden

Die statistische Auswertung der Daten erfolgte mit dem Programm SPSS für Windows (Version 16.0, SPSS Inc.). Als deskriptive Statistiken wurden für quantitative Merkmale Mittelwerte und Standardabweichungen (MW±Stabw.) angegeben. Für kategoriale Daten wurden absolute sowie relative Häufigkeiten (in %) berichtet. Um Unterschiede quantitativer Größen zwischen zwei abhängigen Stichproben zu prüfen wurde der t-Test für verbundene Stichproben verwendet. Bivariate Korrelationen metrischer Merkmale wurden mit Hilfe des Korrelationskoeffizienten nach Pearson (R) bzw. über das Bestimmtheitsmaß (R^2) quantifiziert. Zur Illustration quantitativer Zusammenhänge wurden darüber hinaus Streudiagramme mit Regressions- oder Äquivalenzgeraden (Winkelhalbierende) erstellt. Zudem wurden sowohl univariate wie multivariable Regressionsanalysen durchgeführt. Bland-Altmann-Diagramme dienen zur Veranschaulichung der Übereinstimmung zweier Messverfahren. Mit Hilfe von Quartil-Diagrammen (Box-Plots) und Fehlerbalkengrafiken (Mittelwerte mit 95%iger Konfidenzintervalle) werden Verteilungen quantitativer Untersuchungsgrößen dargestellt. Alle statistischen Auswertungen erfolgten im Sinne einer explorativen Datenanalyse zum zweiseitigen Signifikanzniveau von 5%. Anhand von Diskriminanzanalysen wurde die prädikative Vorhersagekraft einzelner Parameter hinsichtlich der Differenzierung des NYHA Schweregrades untersucht.

8 Ergebnisse und Diskussion

Tabelle 1: Klinischen Daten des Studienkollektivs

	NYHA I	NYHA II	NYHA III	Insgesamt
N	12	19	19	50
Geschlecht	8 Männer (66%) 4 Frauen (33%)	16 Männer (84%) 3 Frauen (16%)	14 Männer (74%) 5 Frauen (26%)	38 Männer (76%) 12 Frauen (24%)
Alter (Jahre)	69,9 ± 4,9	58,1 ± 15,1	58,1 ± 14,8	60,9 ± 14,0
Größe (cm)	170,3 ± 8,3	172,9 ± 8,3	170,0 ± 9,6	171,5 ± 8,8
Gewicht (kg)	78,8 ± 19,0	85,1 ± 12,0	84,8 ± 17,5	83,5 ± 15,9
Pro BNP (pg/ml)	679,0 ± 881,3	1516,5 ± 1071,8	2096,9 ± 1477,2	1536,1 ± 1303,8
LVEF (%)	53,4 ± 7,6	37,1 ± 15,2	33,2 ± 14,6	39,0 ± 15,5
LV Diameter, enddiastolisch (mm)	55,5 ± 7,1	64,2 ± 13,1	70,5 ± 12,1	64,0 ± 12,7
Kreatinin (mg/dl)	1,2 ± 0,2	1,2 ± 0,3	1,4 ± 0,5	1,2 ± 0,4
Triglyzeride (mg/dl)	125,7 ± 37,1	122,3 ± 51,8	220,7 ± 217,8	159,7 ± 142,4
ACE – Hemmer	6 (50%)	14 (74%)	15 (79%)	35 (70%)
ARB	3 (25%)	4 (21%)	5 (26%)	12 (24%)
Beta-Blocker	9 (75%)	17 (89%)	16 (84%)	44 (84%)
Digitalisglycoside	0 (0%)	2 (10%)	7 (37%)	9 (18%)
Phenprocoumon, ASS	8 (66%)	15 (79%)	16 (84%)	39 (78%)
Diuretikum	7 (58%)	15 (79%)	19 (100%)	41 (82%)
Statin	8 (66%)	7 (37%)	10 (53%)	24 (48%)
Protonpumpen-hemmer	4 (33%)	3 (16%)	8 (42%)	15 (30%)
Defibrillator	0 (0%)	6 (32%)	8 (42%)	14 (28%)
Schrittmacher	1 (8%)	2 (10%)	3 (16%)	6 (12%)
DCM	0 (0%)	6 (32%)	8 (42%)	14 (28%)
ICM	12 (100%)	5 (26%)	4 (21%)	21 (42%)

Tabelle 1. LV = linker Ventrikel; LVEF = Ejektionsfraktion; ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; DCM = dilatative Kardiomyopathie; ICM = ischämische Kardiomyopathie;

Ergebnisse der einzelnen Teilstudie werden ausführlich in den beigelegten Veröffentlichungen präsentiert und diskutiert. Es folgt eine kurze Zusammenfassung der wesentlichen Studienergebnisse in Bezug zu den einzelnen Publikationen:

8.1 Jehn M., Schmidt- Trucksäss A., Schuster T., Weis M., Hanssen H., Halle M., Koehler F. Accelerometer based quantification of 6 minute walk test performance in patients with chronic heart failure: applicability in telemedicine. J Cardiac Failure 2009 May; 15(4):334-340.

Kardinale Voraussetzung für das telekardiologische Monitoring der körperlichen Aktivität bzw. Leistung von Patienten mit Herzinsuffizienz mittels Accelerometer ist die möglichst einfache, verlässliche und reproduzierbare Umsetzbarkeit unter Alltagsbedingungen. Zudem muss der Einsatz für klinische Zwecke ausreichend sicher eine Verschlechterung des Aktivitäts- bzw. Leistungszustands des Patienten wiedergeben. Sowohl die Vektormagnitude (RT3) als auch die Schrittzahl stehen in einer engen Beziehung zu der im 6-Minuten Gehtest hinterlegten Wegstrecke. Da die Beziehung durch eine hohe Korrelation der Parameter gekennzeichnet ist, könnte die Messung der Wegstrecke durch die Messung der zurückgelegten Schrittzahl (APM) oder auch der Vektormagnitude (RT3) im 6MWT ersetzt werden. Der Nutzen dieser Parameter liegt in der Unabhängigkeit einer abgemessenen Wegstrecke für den 6MWT. Zudem muss der Patient die Leistung nicht selber messen, da dies von den Geräten übernommen wird. Da der RT3 nicht die Schrittzahl, sondern ein Aktivitätsmaß in Form einer Vektormagnitude misst ist der direkte Vergleich zwischen RT3 und APM nicht möglich. Im Vergleich zu dem Pedometer hingegen, scheint bei niedrigen Gehgeschwindigkeiten ≤ 50 m/min (meist NYHA III - Patienten) nur der APM für die korrekte Erfassung der Schrittzahl geeignet. Der Unterschied in der Schrittzahl war für das Omron-Pedometer im Vergleich zum APM und Handzähler bei den NYHA III Patienten (< 50m/min) statistisch signifikant.

8.2 Jehn M., Schmidt- Trucksäss A., Schuster T., Weis M., Hanssen H., Halle M., Koehler F. Daily walking performance as an independent predictor of advanced heart failure. Am.Heart J. 2009 Feb;157(2):292-8.

Die Alltagsaktivität gemessen mit dem APM Accelerometer scheint sich als Gradmesser des NYHA Schweregrad der Herzinsuffizienz grundsätzlich gut zu eignen. Insbesondere der Parameter *Fast Walk* so wie die tägliche Gesamtgehzeit (min/Tag) sind in ihrer Diskriminationsfähigkeit der NYHA III Patienten mit der ergometrischen VO_2peak gleichwertig zu beurteilen.
Zusammenfassend unterscheidet sich der NYHA Schweregrad III signifikant hinsichtlich der Aktivitätsgruppen *Walk* (> 20 m/min) und *Fast Walk* (> 83 m/min) von NYHA I und II. Eine geringe Aktivitätsdauer bis 10 min pro Tag im Intensitätsbereich *Fast Walk* ist charakteristisch für NYHA III Patienten, über 20 min pro Tag im Intensitätsbereich *Fast Walk* schließen den NYHA Schweregrad III praktisch aus. Die starke Korrelation der mittels Accelerometer gemessenen Leistungsparameter mit der VO_2peak und dem 6MWT zeigt, dass die durchschnittliche Alltagsaktivität ein wesentlicher Indikator für die maximale körperliche Leistungsfähigkeit von Patienten mit Herzinsuffizienz darstellt. Die hohe Diskriminationsfähigkeit von *Fast Walk* bei der richtigen Zuordnung von NYHA III Patienten, ist von hoher klinischer Relevanz bei der Detektion einer klinischen Verschlechterung des Schweregrades der Herzinsuffizienz und könnte zum Beispiel beim telemedizinischen Monitoring von Patienten genutzt werden.

Tabelle 3. Diskriminanzanalyse – Prädikative Vorhersagekraft

	NYHA I	**NYHA II**	**NYHA III**	**Insgesamt**
Schrittzahl 6MWT	66,7 %	47,4 %	47,4 %	52,0 %
Gehstrecke 6MWT	91,7 %	63,2 %	73,7 %	74,0 %
Aktivitätsgruppe *Walk*	75,0 %	31,6 %	68,4 %	56,0%
Aktivitätsgruppe *Fast Walk*	33,3 %	26,3 %	89,5 %	52,0%
VO_2peErgometrie	58,3 %	31,6 %	89,5 %	60,0 %

Tabelle 3. Prädikative Vorhersagekraft der einzelnen Leistungsparameter gemessen anhand einer Diskriminanzanalyse. Der Parameter *Fast Walk* hat zusammen mit der spiroergometrisch ermittelten VO_2peak die stärkste Voraussagekraft hinsichtlich NYHA III Patienten.

8.3 Jehn M., Schmidt- Trucksäss A., Schuster T., Hanssen H., Halle M., Koehler F. Pedometer accuracy in patients with chronic heart failure. Int J Sports Med 2010 Mar; 31:186-191.

Die neue Generation von piezoelektrischen Pedometern wie der Omron HJ-720 ist in seiner Messgenauigkeit stark verbessert worden. Auch ist die eigentliche Körperlage des Pedometers egal, und kann sowohl an der Hüfte als auch in der Brusttasche befestigt werden. Um seine Tauglichkeit bei Patienten mit einem primär geringen Aktivitätsprofil zu untersuchen wurde die Schritterkennungsqualität des Pedometers bei definierten Gehgeschwindigkeiten (40, 50, 60, 70, 80 m/min) auf dem Laufband, im Feldtest und im 6 Minuten Gehtest getestet. Zur Kontrolle wurden die Schritte manuell mit einem digitalem Handzähler mitgezählt.

Hierzu untersuchten wir 97 Patienten mit leichter bis mittelstarker Herzinsuffizienz (NYHA I-III; Alter: 61 ± 13 Jahre). Die Schritterkennung des Pedometers war bei einer Geschwindigkeit > 70 m/min sehr genau (mean bias (% error): 1,0 ± 2,5%; 95% CI: -0,5 to 2,5; *P* = 0,16), jedoch zeigte bei einer Geschwindigkeit ≤ 70 m/min eine zunehmende systematische Abweichung verglichen mit den Handgezählten Schritten (*P* = 0.001). Im 6-Minuten Gehtest zeigte das Pedometer bei den Patienten mit einer Gehstrecke ≤ 350 m / 6 min die stärkste Abweichung (mean bias (% error): 21.3 ± 14.9%; 95% CI: 13.0 to 29.5; *P* < 0.001). Zusammenfassend detektiert das Omron-Pedometer die Schritte nur bei Gehgeschwindigkeiten ≥ 70 m/min ausreichend. Wegen der schlechteren Schritterfassung des Omron-Pedometers bei langsamen Gehgeschwindigkeiten ist es für Patienten mit Herzinsuffizienz NYHA II und III weiniger geeignet.

8.4 Jehn M., Schmidt- Trucksäss A., Weis M., Halle M., Koehler F. Association of physical activity with prognostic measures in elderly patients with heart failure. Journal of Physical Activity and Aging 2009. Under Review.

Zusammenfassend weist die Aktivitätserfassung mittels Aktivitäts-Fragebogen in die gleiche Richtung wie die Langzeitaktivitätserfassung mit dem APM und dem Omron Pedometer über 6 Tage. Je höher die erfragte Aktivität, umso höher ist tägliche Gehzeit (min/day) und die geleistete Schrittzahl. Die Beziehung der Methoden zueinander ist mäßig. Je ausgeprägter die Herzinsuffizienz (NYHA III), desto besser ist die Übereinstimmung zwischen der mittels Fragebogen und APM gemessenen Aktivität, da diese sich bei Patienten mit mittlerer bis schwerer Herzinsuffizienz fast ausschließlich aus Gehen zusammensetzt. Allerdings werden mit dem APM zusätzlich kleine, nicht im Fragebogen erfasste Wegstrecken erfasst, so dass die reine Gehaktivität gemessenen mittels APM besonders deutlich bei den NYHA III Patienten höher ausfällt als die Aktivität des Fragebogens. Hinsichtlich ihrer Aussagekraft auf die maximale Sauerstoffaufnahme und dem Schweregrad der Herzinsuffizienz zeigt die mit dem Accelerometer gemessene Alltagsaktivität eine bessere Korrelation als die mit dem Fragebogen erfasste Aktivität ($R = 0{,}73$ und $R = 0{,}57$, respektive; $P < 0{,}001$). Die gemessene Schrittzahl schnitt in ihrem Bezug zu prognostischen Parametern von allen drei Messmethoden am schlechtesten ab ($R = 0{,}55$; $P = 0{,}001$).

8.5 Jehn M., Schuster T., Weis M., Halle M., Koehler F., Schmidt-Trucksäss A. The six minute walk test: is it a maximum or sub-maximum exercise test in patients with chronic heart failure? European J Appl Physiol 2009 Oct. 107(3):317-323.

Die Korrelation zwischen der ergometrischen VO_2peak und der VO_2peak im 6-Minuten Gehtest ist als hoch einzustufen (R = 0,86; *P* < 0,001). Die VO_{2peak} der NYHA I und II Patienten lag bei der Ergometrie höher als die im 6-Minuten Gehtest erreichte VO_2peak. Bei den NYHA I Patienten war der Unterschied beider Messungen sogar statistisch signifikant (*P* < 0,001). Bei den NYHA III Patienten war es umgekehrt. Hier lag die im 6-Minuten Gehtest gemessene VO_2peak signifikant über der mittels Ergometrie gemessenen VO_2peak (*P* < 0,001). Die VO_{2peak} beider Verfahren sinkt mit zunehmender Schwere der Herzinsuffizienz ab.

Schlussfolgernd deuten dies Ergebnisse an, dass der 6-Minuten Gehtest bei Patienten mit einer ausgeprägten Herzinsuffizienz einen maximalen Leistungstest darstellt, wo hingegen er bei Patienten mit geringen kardialen Einschränkungen nur einen sub-maximalen Leistungstest widerspiegelt.

9 Schlussfolgerung

Die Evaluation des APM Accelerometers lässt sich wie folgt zusammenfassen: Der APM detektiert Schritte auch bei langsamen Gehgeschwindigkeiten ≤ 50m/min zu einem sehr hohen Anteil. Die Schrittzahlen beim standardisierten Gehen auf dem Laufband, der Tartanbahn und im 6-Minuten Gehtest weichen nur gering von der digitalen Handzählung ab. Die Detektionsqualität mit dem APM liegt im Rahmen der klinischen Erfordernisse.

Es bestehen physiologisch sinnvolle Beziehungen zwischen Gehstrecke beim 6-Minuten Gehtest, VO_2peak bei der Fahrradergometrie und der mittels APM erfassten Schrittzahl. Im 6-Minuten Gehtest zeigt die Schrittzahl eine gute Korrelation mit der Gehstrecke im 6-Minuten Gehtest und damit zu einem Parameter, für den die prognostische Wertigkeit bei der Herzinsuffizienz mehrfach nachgewiesen wurde. Somit bietet sich die Schrittzahl als geeigneter Parameter an, der unter den Bedingungen des Telemonitorings erfasst werden kann.

Da sich NYHA III Patienten und NYHA II Patienten im vorliegenden Klientel unterhalb einer Gehstrecke von 400m/6min oder 600 Schritten/6min im 6-Minuten Gehtest nicht mehr überschneiden, ist eine Verschlechterung der Schrittzahl erst bei einem Abfall unter diese Grenze als klinisch diskriminierend im Sinne einer schlechter werdenden Herz-Kreislaufleistungsfähigkeit einsetzbar. Da der klinisch relevante Leistungsbereich im 6-Minuten Gehtest eine Gehstrecke zwischen 240 und 360m/6min determiniert, könnte die im 6-Minuten Gehtest zurückgelegte Schrittzahl als telemedizinisch erfassbarer Parameter zur Beurteilung der Leistungsfähigkeit in Betracht gezogen werden.

In Bezug auf die Alltagsaktivität unterscheidet sich der NYHA Schweregrad III signifikant hinsichtlich der Aktivitätsgruppen *Walk* und *Fast Walk* von NYHA I und II. Eine geringe Aktivitätsdauer bis 10 min pro Tag im Intensitätsbereich *Fast Walk* ist charakteristisch für NYHA III Patienten, über 20 min pro Tag im Intensitätsbereich *Fast Walk* schließen den NYHA Schweregrad III praktisch aus. Für die Vorhersage des NYHA-Schweregrades (Diskriminanzanalyse) ist

die Gehstrecke im 6-Minuten Gehtest mit 72,4 % richtiger Zuordnung der Gruppenzugehörigkeit im gesamten untersuchten Klientel am besten geeignet. Betrachtet man alleine die vorhergesagte Gruppenzugehörigkeit der NYHA III Patienten, so ist die Disikriminationsfähigkeit der Aktivitätsgruppe *Fast Walk* (89,5%) der ergometrisch ermittelten VO_{2peak} (89,5%) in ihrer Vorhersagekraft gleichgestellt. Demgegenüber ist die Gehstrecke im 6-Minuten Gehtest bei der Zuordnung der NYHA III Patienten nur mäßig geeignet (68,6 %) und die Schrittzahl im 6MWT schneidet wegen deutlicher Überschneidung von NYHA II und III oberhalb einer Schrittzahl von 600/6min im 6MWT mit 54,3% richtig vorhergesagter NYHA III Patienten am schlechtesten ab.

Die Aktivitätserfassung mittels Aktivitätsfragebogen weist in die gleiche Richtung wie die Langzeitschritterfassung mit dem APM und Omron Pedometer über 6 Tage. Je höher die erfragte Aktivität, umso höher ist die hinterlegte Gesamtgehzeit (total walking time in min/day) und die geleistete Schrittzahl. Die Beziehung der Methoden zueinander ist mäßig. Damit wird die grundsätzliche Eignung der Gehzeit und der geleisteten Schrittzahl als Langzeitaktivitätsmaß anhand eines validierten Aktivitätsfragebogen dokumentiert.

Da es sich bei den genannten Teilstudien um Querschnittsuntersuchungen handelt, kann über die klinische Wertigkeit der Aktivitätserfassung mit dem APM als Prognoseparameter für Patienten mit Herzinsuffizienz erst in einer Längsschnittuntersuchung eine schlüssige Aussage gemacht werden. Sowohl die hinterlegte Schrittzahl im 6MWT als auch die Alltagsaktivität scheinen dafür geeignete Parameter zu sein. Dennoch sollten die hier präsentierten Ergebnisse in einem größeren Studienkollektiv belegt werden.

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11 APPENDIX

11.1 Jehn M., Schmidt- Trucksäss A., Schuster T., Weis M., Hanssen H., Halle M., Koehler F. Accelerometer based quantification of 6 minute walk test performance in patients with chronic heart failure: applicability in telemedicine. J Cardiac Failure 2009 May; 15(4):334-340.

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Daily walking performance as an independent predictor of advanced heart failure: Prediction of exercise capacity in chronic heart failure

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Purpose The purpose of this study was to use an accelerometer to measure daily walking performance in patients with chronic heart failure (CHF) to investigate if this parameter is a determinant of New York Heart Association class and indicative of maximal and functional exercise capacity.

Methods Fifty patients with CHF were instructed to wear an accelerometer for 7 consecutive days while going about their daily business. Maximal and functional exercise capacity was assessed by cardiopulmonary (VO_{2peak}) and 6-minute walk testing, respectively.

Results Patients in New York Heart Association I, II, and III reached an average total walking time (TWT) of 160.6 ± 35.8 minutes, 133.9 ± 59.0 minutes, and 76.1 ± 22.5 minutes per day of which 19%, 19%, and 9% where spent in the fast walking mode (>83 m/minute), respectively. The TWT correlated strongly with VO_{2peak} ($r = 0.72$; $P < .001$) and 6-minute walk testing distance ($r = 0.68$; $P < .001$). The TWT and time spent in fast walking mode were the strongest determinants in discriminating moderate CHF.

Conclusion Daily walking performance is a clear determinant of maximal and functional exercise capacities in patients with CHF. Walking intensity in particular is an independent predictor in discriminating patients with advanced heart failure. Monitoring of daily walking performance might aid in detecting disease progression and improve clinical outcome. (Am Heart J 2009;157:292-8.)

Exercise capacity is a strong predictor of mortality in patients with chronic heart failure (CHF).[1] Patients suffer from cardiopulmonary and musculoskeletal limitations that greatly reduce their ability to exercise and impede on their quality of life.[2] Consequently, a marked decrease in maximal oxygen consumption (VO_{2peak}) and exercise tolerance during the 6-minute walk test (6 MWT) is observed, depending on the severity of heart failure. These parameters are tightly linked to clinical prognosis and mortality in patients with CHF.[3,4]

Daily physical activity is believed to attenuate disease progression and improve survival rate among patients with CHF.[5,6] Questions concerning the amount of stairs possible and distance walked before feeling the sensation of dyspnea and/or syncope are usually implied to help clinicians categorize patients with CHF into New York Heart Association (NYHA) functional classes I-IV. In addition, the use of the 6 MWT offers objective measures of functional capacity in this patient population. It is less time consuming than cardiopulmonary exercise testing and thought to be a better reflection of the patient's true functional limitation and short-term mortality risk.[7]

Monitoring of habitual walking activity might offer additional useful information to clinically assess functional status in patients with CHF. In addition, it allows for day-to-day fluctuations to be taken into account which periodically done cardiopulmonary exercise stress tests do not. Performance is evaluated in terms of routine activities as opposed to test-specific expectations and abilities. A study by Walsh et al,[8] demonstrated daily

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activity levels, or more specifically inactivity in daily life, to be a better indicator of disease prognosis and mortality than cardiopulmonary exercise testing.

Using accelerometers to assess activity levels in free living conditions is becoming increasingly popular, and many studies have used this tool to gain insight into habitual activities within a population sample in the young and the healthy.[9-11] In addition, more and more clinical trials are relying on these tools to investigate the positive relationship between habitual physical activity and disease progression and/or the effect of a physical activity program as primary or secondary prevention in the patient's rehabilitation process, for example, in chronic lung disease, cancer, type II diabetes.[12-18]

The purposes of this study were therefore to assess habitual walking performance in patients with CHF by means of an accelerometer and to investigate if this information is clinically useful to distinguish NYHA functional class. Moreover, we wanted to evaluate if habitual walking performance is a determinant of functional and maximal exercise capacity.

Methods

Patient recruitment

Subjects were recruited via an advertisement in the local newspaper and with the cooperation of a heart failure outpatient clinic at the local university hospital. Inclusion criteria were mild to moderate stable heart failure defined by NYHA class I-III, regardless of age and medical history, and willingness to participate in clinical and laboratory analyses. Exclusion criteria were any unstable medical conditions that were contraindicative to exercise testing or if patients were unable to walk without assistance. This study complies with the Declaration of Helsinki and was approved by the ethics committee. Name of the project is "TIM-HF Studie," and it is registered under www.clinicaltrials.gov, NCT00543881. All patients signed an informed consent before being examined and categorized according to their NYHA functional status. A total of 50 patients with heart failure (n = 10 NYHA I, n = 20 NYHA II, and n = 20 NYHA III) were defined in the study protocol and recruited based on questioning of self perceived exercise capacity. Patients underwent medical history and in-depth physical examination including echocardiogram, resting electrocardiogram (ECG), and NT-proBNP before exercise testing. A cardiopulmonary exercise stress test on the bicycle ergometer (VO_{2peak}) and a 6 MWT were performed to assess maximal and functional exercise capacity, respectively. Based on clinical data as well as self-reported exercise tolerance, each patient was reclassified by 2 independent physicians blinded to the results of $V0_{2peak}$, 6 MWT, and accelerometer testing to exclude potential bias on walking performance. This classification resulted in a study population of 12 NYHA I patients, 19 NYHA II patients, and 19 NYHA III patients.

Bicycle ergometer

Each subject undertook a symptom-limited cardiopulmonary exercise test (ramp protocol, start 10 W, increment 10 W m^{-1}) using an electronically operated cycle ergometer (Sport Excalibur, Lode Medical technology, Groningen, the Netherlands). The test was performed in an air-conditioned laboratory with an ambient room temperature of 21°C and humidity of 30% to 40 % in the early afternoon under nonfasting conditions. Subjects were encouraged to exercise to exhaustion or until cardiac arrhythmias developed. Exhaustion was defined by muscular leg fatigue and/or breathlessness. Subjects wore a plastic face mask to which a mouth piece was connected and respiratory gases were collected and analyzed via ZAN metabolic cart (ZAN 600 USB CPX, nSpire Health GmbH, Oberthulba, Germany). VO_2 and VCO_2 were measured every 10 seconds, and peak oxygen consumption (VO_{2peak}) was defined as the highest oxygen consumption reached during the exercise test. Heart rate was measured on a 12-lead ECG, and the ECG was monitored continuously. Blood pressure was measured at rest, in 1-minute intervals at the end of each exercise stage, and in 2-minute intervals during the recovery phase. Perceived exertion using the Borg scale was recorded at the end of each stage. Five minutes of recovery followed the exercise bout in which the patient was instructed to keep peddling at 25 W resistance to prevent blood pooling and/or arrhythmias. Upon completion of recovery, the patient was allowed to dismount the bicycle and told to rest for 60 minutes before starting the 6 MWT. Bicycle ergometer test and 6 MWT were administered in randomized order.

The 6 MWT

The 6 MWT was conducted in an enclosed corridor on a measured course that was 40 m long. The course was marked every 5 m, and subjects were instructed to walk from one end to the other end, covering as much distance as possible during the 6 minutes. Remaining time was called every minute, and subjects were allowed to rest if needed. The accelerometer (Meddlogger, Aipermon GmbH, Munich, Germany) was mounted onto the left hip to compare detected steps during the 6 MWT with steps counted by digital hand counter (HC-1, Voltcraft, Hirschau, Germany). Data from the accelerometer were downloaded onto the computer via USB cable and saved. A special program (Analysis Viewer, Aipermon) was used to open the files and view its contents.

7-day activity assessment

Patients were given an accelerometer (Aipermon GmbH) to wear at home while going about their daily business. The device was attached to the patient's belt on the left hip, and patients were instructed to wear the device for at least 12 hours a day for 8 consecutive days. The accelerometer was to be attached upon rising in the morning and only to be taken off for showering, bathing, and sleeping. Since the first and last day (days where device was received and returned) were not complete days, these days were excluded from the analysis, and only 6 full days were used. All device settings (date, time, weight, age, and gender) were preprogrammed for each patient upon receiving it, and the device was switched on throughout the entire measurement period to keep patient handling of the accelerometer to a minimum. Upon return, the data were copied onto a PC, and its contents viewed via ActiCoach MPAT2Viewer (Aipermon, GmbH). Patients were then asked to complete a brief questionnaire that evaluated their compliance and their opinion about wearing the accelerometer in the future. Total times (minutes

Table I. Patient characteristics and exercise data

	NYHA I	NYHA II	NYHA III	Total	P*
n	12	19	19	50	
Gender					
Men	8 (66)	16 (84)	14 (74)	38 (76)	
Women	4 (33)	3 (16)	5 (26)	12 (24)	
Age	69.9 ± 4.9†	58.1 ± 15.1	58.1 ± 14.8‡	60.9 ± 14.0	<.05
Height (cm)	170.3 ± 8.3	172.9 ± 8.3	170.0 ± 9.6	171.5 ± 8.8	.72
Weight (kg)	78.8 ± 19.0	85.1 ± 12.0	84.8 ± 17.5	83.5 ± 15.9	.85
VO_{2peak} (mL/kg† per minute)	26.6 ± 4.1§	23.1 ± 6.2‖	14.1 ± 2.8‡	20.5 ± 6.9‡	<.01
6 MWT distance (m)	633 ± 60.4†	555 ± 76.6‖	387 ± 93.3‡	510 ± 129	<.01
EF %	53.4 ± 7.6†	37.1 ± 15.2¶	33.2 ± 14.6‡	39.0 ± 15.5	<.01
LV diameter (mm)	55.5 ± 6.2§	64.2 ± 11.5¶	70.5 ± 11.0‡	63.4 ± 12.3	<.01
NTpro BNP	679.0 ± 881.3	1517 ± 1072	2097 ± 1477‡	1536 ± 1304§	<.01
ACE inhibitor	6 (50)	14 (74)	15 (79)	35 (70)	
ARB	3 (25)	4 (21)	5 (26)	12 (24)	
β-Blocker	9 (75)	17 (89)	16 (84)	44 (84)	
Phenprocoumon, ASA	8 (66)	15 (79)	16 (84)	39 (78)	
Diuretic	7 (58)	15 (79)	19 (100)	41 (82)	
DCM	0 (0)	6 (32)	8 (42)	14 (28)	
ICM	12 (100)	5 (26)	4 (21)	21 (42)	

Clinical characteristics of study population. Data are presented as means ± SD or number (percentage). *EF*, Ejection fraction; *LV*, left ventricular function (diastolic); *ACE inhibitor*, angiotensin-converting enzyme inhibitor; *ARB*, angiotensin receptor blocker; *ASA*, acetylsalicyl acid; *DCM*, dilated cardiomyopathy; *ICM*, ischemic cardiomyopathy.
#Overall group comparison by analysis of variance/χ^2 test; post hoc group differences with $P < .05$.
†NYHA I versus NYHA II.
‡NYHA III versus NYHA I.
§NYHA I versus NYHA II.
‖NYHA II versus NYHA III.
¶NYHA II versus NYHA III.

per day) spent passively (PAS), actively (ACT), walking (WLK), and fast walking (FWLK) were analyzed. Walking and FWLK times were computed to a total walking time (TWT). Activity modes and accelerometer detection accuracy were extensively validated, and detailed results are reported elsewhere. In summery, the device was able to accurately detect steps to 99% at walking speeds ranging as low as 20 m/minute onward. There was a 3-second detection delay in recognizing changes in activity modes. For the scope of this study, we compared accelerometer detected steps with steps counted by digital hand counter during the 6 MWT and found a strong correlation between both measurements ($r = 0.99$, $P < .001$). Mean difference was not statistical significant with mean 0.1 ± 2.0 ($P = .7$).

Data analysis

Statistical analysis was done using SPSS software (version 15.0, SPSS Inc.).

Data were descriptively analyzed reporting mean ± SD for quantitative measurements and percentages for frequencies. Bivariate correlations of continuous variables were investigated using Pearson correlation coefficient (r). Statistical comparisons between 2 related measurements were assessed by paired Student t test. Discriminant analysis was performed to identify the prediction strength of activity parameters on NYHA classification. Further, receiver operating characteristics (ROC) analyses were performed to determine optimal cutoff values providing highest accuracy in prediction of NYHA III class. Area under the ROC curve (AUC) as well as sensitivity and specificity levels were calculated and reported comparatively. In all data analyses, P values less .05 were considered as statistically significant.

Results

Patient characteristics

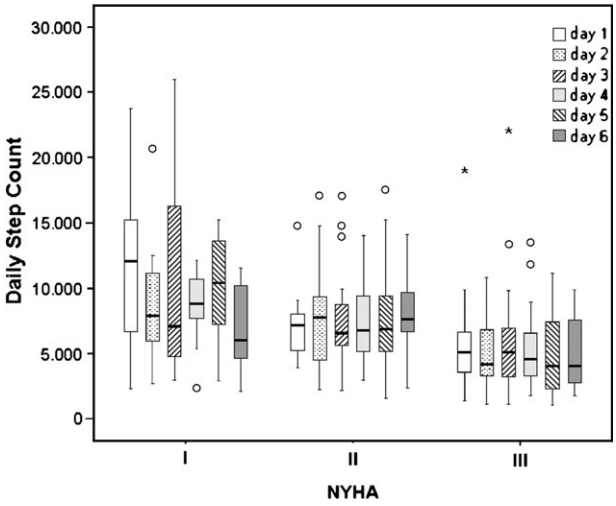
All clinical and exercise data are listed in Table I. The mean age of all subjects (38 [76%] men and 12 [24%] women) was 60.9 years. Mean VO_{2peak} and ejection fraction was 20.5 mL/kg per minute and 39%, respectively. Most patients were taking angiotensin-converting enzyme inhibitor, β-blockers, and a diuretic. Fifty percent of the patients had an internal defibrillator and/or a pacemaker. All patients completed the tests, and we observed no medical problems during exercise testing (ie, severe cardiac arrhythmias).

6-Day accelerometer activity

Daily activity, measured in terms of steps per day are depicted in Figure 1.

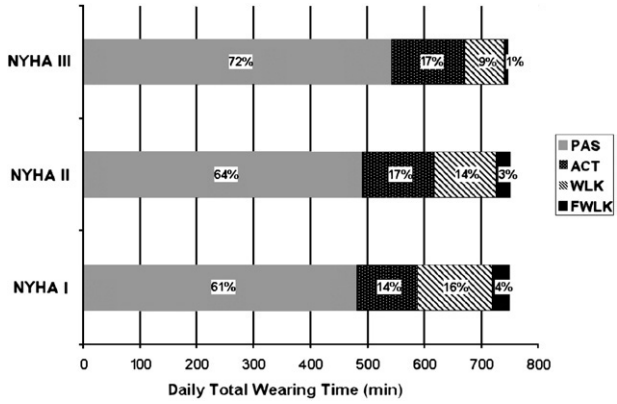
Walking speeds from 0 to 80 m/minute were detected as *walking*, and walking speeds from 83 to 115 m/minute were detected as *fast walking*. Speeds >115 m/minute were considered *sportive* at which point walking would turn into jogging in most individuals. However, the latter was not relevant for this study population. Accelerometer output is shown as percentage of time spent in different activity modes based on

Figure 1



Daily mean accelerometer step count according to NYHA class based on 6 days of accelerometer output: n = 12, NYHA I; n = 19, NYHA II; and n = 19, NYHA III. The spots represent outliers (values between 1.5 and 3 box lengths from the upper or lower edge of the box); the stars represent extreme outliers (values >3 box lengths).

Figure 2



Percentage of times spent in different accelerometer activity modes based on the total daily wearing time (minutes) and separated by NYHA class.

total wearing time (12.82 ± 1.44 hours/day) according to NYHA functional class (Figure 2).

All raw activity data (minutes) are listed in Table II.

Activity modes

The TWT correlated strongly with VO_{2peak}, 6 MWT distance, and NYHA classification ($r = 0.72$, $P < .001$; $r = 0.68$, $P < .001$; $r = -0.65$, $P < .001$, respectively) and was the strongest determinant in discriminating NYHA III patients (94%). Time spent in PAS mode was significant for NYHA III ($P < 05$), but its overall prediction strength was low (38%). Active time was not predictive of NYHA class and did not significantly correlate with any of the investigated parameters. The difference in mean TWT, WLK, and FWLK was statistically significant for NYHA II and NYHA III ($P = .001$) and for NYHA I and III ($P < .001$), however not for NYHA I and II ($P = .1$).

Time spent in FWLK mode (19%, 19%, and 9% of TWT and 4%, 3%, and 1% of overall daily wearing time for NYHA I, II, and III, respectively) was also a strong determinant along with VO_{2peak} in discriminating moderate heart failure (sensitivity: NYHA III = 89.5%). Seventy-nine percent of NYHA III patients spent 0 to 10 minutes in the FWLK speed, and only 4 of 19 NYHA III patients (21%) had an average FWLK time >10 minute per day. All 19 patients were <20 minute per day, and the difference was statistically significant compared to NYHA I and II, who could not be distinguished based on this parameter. Time spent in WLK modus and steps per day was less predictive (sensitivity: NYHA III = 68% and 74%, respectively) (Table III). Overall, 6 MWT distance was the strongest predictor in placing all groups correctly (74%).

The activity times per day (minutes) spent in the WLK and FWLK modus were added successively to check to what extent the statistical predictive strength for WLK and FWLK (based on the accuracy of prediction NYHA = III) is dependent on the sum of absolute times spent in these activity modes within different time frames. In other words, how many days of monitoring are needed to identify or exclude NYHA III based on the parameters WLK and FWLK. The ROC analyses revealed several cutoff points of summarized walking parameters within the 6-day period of investigation (Table IV).

The strength to discriminate NYHA III patients based on the parameters WLK and FWLK increased with increasing monitoring days. Four days of monitoring are needed for the parameter FWLK to obtain a sensitivity and specificity value of 84% (NYHA = III or NYHA ≠ III). Five days of monitoring are needed for the parameter WLK to obtain a sensitivity value of 95% and specificity value of 74% (NYHA = III or NYHA ≠ III). The AUC for correctly classifying patients with moderate heart failure based on the parameter FWLK (Table IV) was slightly lower than for VO_{2peak} (AUC = 0.96) and 6 MWT distance (AUC = 0.95). The differentiation of NYHA class based on the sum of times (minutes) spent in the FWLK and WLK activity modus (4 and 5 monitoring days, respectively) are illustrated in Figures 3 and 4.

Discussion

The key finding of this study is that daily time attributed to FWLK is a clinically useful measure to identify patients with advanced heart failure. Of all investigated

Table II. Accelerometer output activity data

	NYHA I	NYHA II	NYHA III	Total	*P**
n	12	19	19	50	
PAS (m)	480.2 ± 47.3	489.7 ± 84.6†	542.4 ± 69.4‡	507.5 ± 75.3	.031
ACT (m)	107.4 ± 22.3	126.8 ± 52.1	127.2 ± 63.5	122.3 ± 51.6	.53
WLK (m)	129.9 ± 22.6	107.6 ± 43.1§	70.2 ± 21.4‖	98.7 ± 40.3	.001
FWLK (m)	30.7 ± 26.4	26.3 ± 26.2†	6.6 ± 6.1‖	20.0 ± 23.1	.004
TWT (WLK + FWLK)	160.6 ± 35.8	133.9 ± 59.0§	76.8 ± 22.5‖	118.7 ± 54.6	.001
% FWLK/TWT	19%	19%†	9%‡	0.14 ± 0.11	.04
Steps per day	9466 ± 3362	7687 ± 2726†	5431 ± 2650‖	7257 ± 3226	.001

Average time spent per day (minutes) in different accelerometer activity modes.
*Overall group comparison by analysis of variance/χ^2 test; post hoc group differences with $P < .05$.
†NYHA II versus NYHA III.
‡NYHA III versus NYHA I; $P < .005$.
§NYHA II versus NYHA III.
‖ NYHA III versus NYHA I.
¶NYHA I versus NYHA II.
#NYHA I versus NYHA II.

Table III. Discriminate analyses—accuracy of prediction

	NYHA I	NYHA II	NYHA III	Total
Steps per day	50.0%	36.7%	73.7%	50.0%
TWT	58.3%	15.8%	94.7%	56.0%
WLK	75.0%	31.6%	68.4%	56.0%
FWLK	33.3%	26.3%	89.5%	52.0%
6 MWT Distance	91.7%	63.2%	73.7%	74.0%
VO_{2peak}	63.6%	36.8%	89.5%	63.3%

Discriminate analysis; prediction strength of different parameters to categorize patients into correct NYHA class.

parameters, time spent in FWLK was the strongest determinant, besides TWT and equal to VO_{2peak}, in correctly classifying patients with moderate to severe heart failure (NYHA III). Moreover, TWT was indicative of NYHA functional class because patients with NYHA III spent considerably less time walking and more time passively throughout the day compared to NYHA I and NYHA II patients. The close correlation of TWT with VO_{2peak} and 6 MWT distance demonstrates that daily walking activity or inactivity per se are strong determinants of functional and maximal exercise capacities.

Several other studies have used conventional exercise testing parameters to predict daily activity levels in patients with varying degrees of diseases. Pitta et al[16,19] showed 6 MWT distance to be the strongest independent predictor of inactivity in chronic obstructive pulmonary disease patients. Witham et al[20] used a similar model to explore the association of exercise capacity and daily activity levels in frail, elderly heart failure patients and also found that 6 MWT distance was the only consistent predictor of daily activity levels in this studied subgroup. However, this is the first study to use habitual walking performance to discriminate patients with moderate heart failure and demonstrate its predictive strength in terms of functional and maximal exercise capacities.

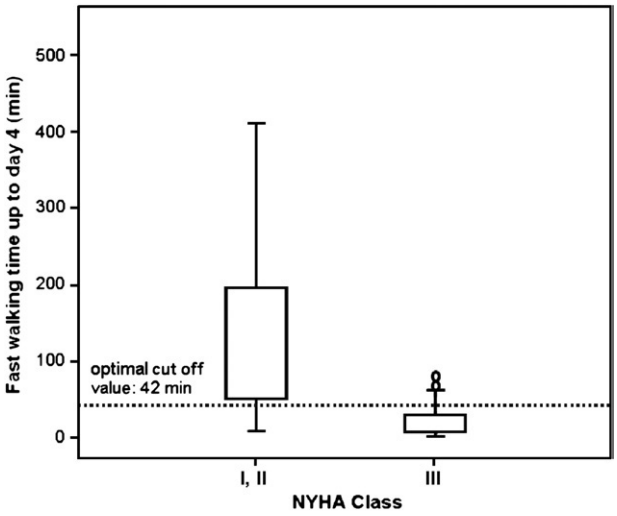
Table IV. Sensitivity and specificity of TWT and total FWLK according to single monitoring days

	AUC	Cutoff value*	Sensitivity	Specificity
Total WLK up to day:				
1	0.79	83	0.89	0.61
2	0.80	150	0.68	0.84
3	0.82	273	1.00	0.58
4	0.80	356	0.95	0.65
5	0.84	433	0.95	0.74
6	0.83	539	1.00	0.65
Total FWLK up to day:				
1	0.87	11	1.00	0.61
2	0.89	22	0.95	0.71
3	0.88	35	0.89	0.77
4	0.89	42	0.84	0.84
5	0.90	50	0.84	0.84
6	0.91	57	0.84	0.87

*Optimal cutoff value determined by ROC analyses, patients with values less or equal to * are classified to NYHA III.

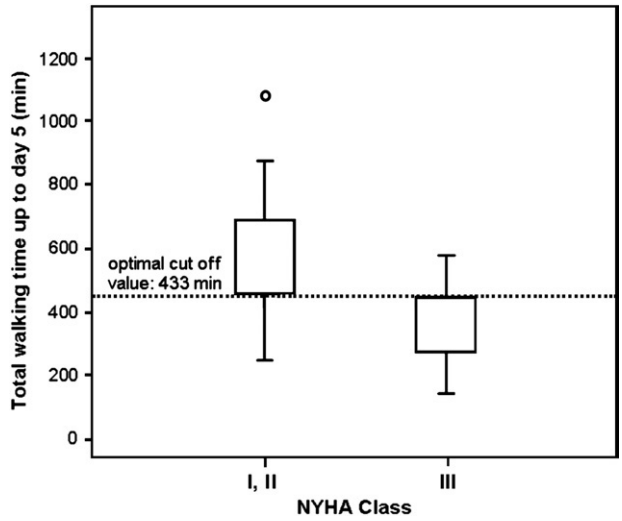
The single times (minutes) per day spent in the activity modus FWLK and WLK were added successively to obtain the amount of monitoring days required to identify or exclude NYHA III based on the total sum of times for each parameter. As to be expected, the prediction strength increased with increasing monitoring days (higher total sum for FWLK and WLK minutes). Our analysis showed that 4 days of monitoring for the parameter FWLK and 5 days for the parameter WLK are needed to obtain sensitivity and specificity values high enough to distinguish patients with moderate to severe heart failure (NYHA III). Although higher sensitivity values than total FWLK time, TWT showed less specificity with nonstrictly monotonous increments over time. Compared to VO_2peak and 6 MWT, FWLK had a marginally lower accuracy of prediction (AUC) of correctly identifying NYHA III patients. However, habitual walking performance seems to have an

Figure 3



Successive summation of time (minutes) in FWLK modus needed to differentiate NYHA class based on total FWLK. Four days of monitoring is needed.

Figure 4



Successive summation of time (minutes) in WLK modus needed to differentiate NYHA class based on TWT. Five days of monitoring is needed.

intuitive attraction as a more realistic measure of exercise capacity than laboratory tests and might prove useful in clinical practice.

A study by Trost et al[11] also investigated the minimal monitoring days needed for accelerometers to access usual physical activity in children and concluded that 7 days of monitoring are required to provide reliable estimates of typical daily activity levels in this study population. Contrarily to our study, however, a uniaxial accelerometer was used, which is less sensitive than a triaxial accelerometer and might account for the increased monitoring days necessary to distinguish typical activity patterns. In addition, children or adolescents do not have the same stringent daily routines typically seen in elderly individuals. In a study by Pitta et al, a triaxial accelerometer was used to measure daily activity levels in chronic obstructive pulmonary disease patients, and results showed that 2 days of assessment were sufficient to achieve an intraclass reliability coefficient of >0.7, the minimal value required for the reliability of a variable among a group of individuals to be considered acceptable.[16]

The relatively high daily walking times accumulated by NYHA III patients are most likely due to the severe physical limitations these patients face in daily life resulting in extremely slow walking intensities. The finding that NYHA III patients only spent an average of 6.5 minute per day in the FWLK mode, equivalent to 9 % of TWT, supports this assumption and strengthens the hypothesis that in addition to walking performance (TWT), walking intensity is decisive in terms of clinical prognosis.

Daily walking activity, in terms of steps per day, did not vary considerably between days, except in NYHA I patients who showed a '1 day on/1 day off' pattern with walking activity peaking every other day. Most NYHA I patients did participate in a cardiac rehabilitation 1 to 2 times per week, whereas NYHA II and III did not participate in any organized extracurricular activities. To exclude an effect of the cardiac rehabilitation class on study outcome, we repeated the analysis excluding the time of the rehabilitation class (90 minutes of ~78 hours total monitoring time) in those individuals who participated in it during the week they had the accelerometer (6 of 12 NYHA I). This had no significant effect on study outcome.

Regarding the accelerometer's practical applicability, it is noteworthy that the patient compliance to wear the accelerometer in this study was 100%. Moreover, patients reported feeling encouraged to increase their amount of physical activity during the week they had the accelerometer. Fear of cardiac events was the main reason given by patients with moderate heart failure when asked why they kept physical activity to a minimum.

In conclusion, using an accelerometer to monitor daily walking performance in patients with CHF might prove to have additional value in evaluating exercise programs and measuring sequential changes in a patient's condition. In this study, walking intensity was a strong determinant of moderate to severe NYHA functional status. In addition, daily walking performance in terms of TWT is an indicator of functional and maximal exercise capacities. This type of patient monitoring may be taken

into consideration in the initial assessment of patients with CHF. If the results of this pilot study are underlined by a broader data basis, it might substitute cardiopulmonary exercise testing and/or allow for changes in exercise tolerance to be monitored over a longer time frame in suitable clinical cases.

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Accelerometer-Based Quantification of 6-Minute Walk Test Performance in Patients With Chronic Heart Failure: Applicability in Telemedicine

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ABSTRACT

Background: Distance walked in the 6-minute walk test (6MWT) is an important prognostic parameter used clinically to assess functional status in patients with chronic heart failure (CHF). In this study, we investigated if alternative performance parameters with similar prognostic value can be gained from accelerometers.

Methods and Results: Fifty CHF patients (age, 60.9 ± 14.0 years) were asked to perform a 6MWT while wearing 2 accelerometers and 1 pedometer. Total 6MWT step frequency (SF) and activity counts (VMU) were correlated to 6MWT distance. The accelerometer was highly accurate at quantifying SF (detected vs. observed: $r = 0.99$; $P < .001$), whereas the pedometer was unreliable below 50 m/min. VMU increased linearly with walking speed ($r = 0.99$), and both SF and VMU correlated strongly with 6MWT distance (VMU: $r = 0.91$; SF: $r = 0.87$, respectively; $P < .001$) and each other ($r = 0.80$, $P < .001$).

Conclusions: Accelerometers are reliable in measuring physical performance during the 6MWT in CHF patients. Besides the simple acquisition of 6MWT distance currently used for patient assessment, accelerometers provide new data that might be useful to evaluate exercise performance during the 6MWT. This allows for routine assessment of exercise capacity in a home-based setting in the context of telemedicine. (*J Cardiac Fail 2009;15:334−340*)

Key Words: Activity monitoring, RT3, step frequency, 6-minute walk test.

Patients with chronic heart failure (CHF) are characterized by a poor exercise tolerance prohibiting them to manage daily routine without limitation.[1] A marked decrease in exercise capacity usually indicates acute health deteriorations thereby increasing hospitalization and mortality risk.[2−6] Thus exercise capacity is an essential prognostic parameter in CHF patients and requires close monitoring.

Exercise capacity in CHF patients is typically assessed by means of objective performance testing such as cardiopulmonary exercise testing (VO_2peak) done either on a bicycle ergometer or treadmill.[7−9] Alternatively, the 6-minute walk test (6MWT) is commonly used to assess functional exercise capacity in this patient population because it is less time consuming than a cardiopulmonary exercise test and does not require elaborate equipment or technically trained personnel.[10,11] By nature being a constant load walking test during which patients choose their own walking intensity, the 6MWT is thought of by many to be a better reflection of the patient's true ability to function in routine daily activities.[12]

Standardized exercise tests are generally only done in an in-hospital or outpatient setting during allocated appointment times. If decreases in exercise capacity occur in the interim, health deteriorations might progress unnoticed.[13] For this reason, the concept of telemedical patient

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Conflict of interest: The manufacturers of the APM provided all activity measurement instruments at no cost for evaluation purposes.

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monitoring is rapidly gaining in interest among health care professionals. Several commercially available accelerometers and pedometers are equipped with USB cables and elaborate computer programs allowing patients to download their exercise data onto the computer and print detailed reports quantifying their daily activity levels and periods of inactivity or even sleep.

However, most of these devices are designed primarily for a young and healthy population and intended for identifying movement intensities ranging from light to vigorous exercise. To our knowledge, only a few technologies are precise at detecting low range movement intensities and therefore are most are unsuitable for patients with severe functional limitations (<300 m/6 min; ≤4 METS) typically seen in the elderly and/or patients with moderate to severe heart failure.[14–16]

Therefore, the purpose of this study was to evaluate the efficacy of accelerometers including pedometers to detect and quantify the amount of physical activity in patients with CHF during the 6MWT. In this context, we investigated if accelerometers offer additional information on 6MWT performance that can be used to identify heart failure severity. This would allow for clinically implementing theses devices into an outpatient or home-based setting to routinely assess exercise capacity and thereby advance the concept of telemedical patient monitoring.

Methods

Patient Recruitment

Subjects were recruited with the cooperation of a heart failure outpatient clinic at the local hospital. Inclusion criteria were mild to moderate stable heart failure defined by New York Heart Association (NYHA) Class I-III, regardless of age and medical history or willingness to participate in clinical and laboratory analyses. Exclusion criteria were any unstable medical conditions that were contraindicative to exercise testing or if patients were unable to walk without assistance. The study complies with the Declaration of Helsinki and was approved by the local university's ethics committee. All patients signed an informed consent. A total of 50 heart failure patients (n = 10 NYHA I, n = 20 NYHA II, and n = 20 NYHA III) were defined in the study protocol. NYHA class was initially assigned by their primary care physician based on self-perceived exercise tolerance and a current cardiopulmonary exercise stress test on the bicycle ergometer. Data also included medical history, echocardiogram, and resting electrocardiogram. Based on clinical data, each patient was repeatedly classified by 2 independent physicians blinded to the results of the initial classification, 6MWT, and accelerometer testing. This classification yielded a study population of n = 12 NYHA I, n = 19 NYHA II, and n = 19 NYHA III.

Sample Size

With a total sample size of 50 patients, the study was powered to establish a correlation between 6MWT distance and accelerometer detected steps of at least $r = 0.80$ (Pearson correlation coefficient) with 80% probability at a 1-sided confidence level of 95%, assuming an actual underlying correlation of about $r = 0.90$.

Exercise Testing

Field Walking Test. To test the devices accuracy in recording step frequency, patients were asked to walk on a paved test course at 40, 50, 60, 70, and 80 m/min for 6 minutes per stage. On the right hip they wore a common pedometer (OMRON, Walking style Pro) and the accelerometer RT3 (Stay Healthy, USA); on the left hip, they wore the accelerometer APM (Medlogger, Aipermon GmbH, Germany). Both accelerometers were 3-dimensional compared with the 1-dimensional pedometer. An assistant blinded to the study counted steps manually by digital hand counter (HC-1, Voltcraft, Hirschau, Germany) as reference for step accuracy. The test course was marked every 5 meters and subjects were instructed to adapt their gait to acoustical signals that were given every 5 meters to indicate walking speed. The time gaps between each acoustic signal decreased with increasing walking speed, which, in turn, increased every 6 minutes until 80 m/min was reached.

6-MWT. The 6MWT was conducted in an enclosed corridor on a measured course that was 40 m long. The course was marked with red triangular hats every 5 m, and subjects were instructed to walk from 1 end to the other end, covering as much distance as possible during the 6 minutes. Subjects were allowed to rest if needed and remaining time was called every minute. The accelerometers were attached in exactly the same fashion as previously described. Again, steps were counted by digital hand counter as reference for step frequency and 6MWT distance was recorded on test completion. The same assistant from the calibration test also counted steps during the 6MWT. Data from each of the accelerometers were downloaded onto the computer via USB cable and activity data were analyzed with the device's corresponding software (Analysis Viewer, Aipermon). To check the reproducibility of outcome measures patients (n = 45) were asked to repeat the 6MWT after a 1-hour break. During the second 6MWT, steps were counted by a second assistant blinded to the results of the first 6MWT.

Data Analysis

Statistical analysis was done using SPSS software (version 15.0, SPSS Inc). Data were descriptively analyzed reporting mean ± standard deviation (SD) for quantitative measurements. Bivariate correlations of continuous variables were investigated using Pearson correlation coefficient (r). Scatter charts including linear regression lines as well regression equations were provided to illustrate and quantify correlations of relevant measurements. The chi-square test was used to compare frequencies between independent samples. To reduce multiple test issues, pair wise group comparisons via t-test were only conducted if overall comparisons by analysis of variance were statistically significant. In all data analyses, P values less than .05 were considered as statistically significant and were reported in an explorative manner. Reproducibility of 6MWT data was assessed by repeated measures analysis of variance followed by Bland-Altman analysis in which individual test differences were plotted against their means. Mean bias and 95% confidence interval was calculated as mean ± 1.96 SD of between test differences.

Results

Patient Characteristics

The classification of all study participants resulted in a study population of n = 12 NYHA I, n = 19 NYHA II,

and n = 19 NYHA III. The mean age of all subjects was 60.9 years; 76% were men. There was no statistical evidence of different gender distributions among NYHA groups. All patients completed the tests and we observed no major clinical problems. Seven or 12 NYHA I patients were diagnosed with HF and preserved ejection fraction, compared with NYHA II and III who suffered from heart failure and systolic dysfunction (Table 1).

Step Accuracy

The 3-dimensional accelerometer (APM) was highly accurate at detecting steps, and readings correlated strongly with hand-counted steps, regardless of walking speed during field test analysis ($r = 0.99$, $P < .001$). The pedometer was good at detecting steps at walking speeds ≥50 m/min, yet was unreliable below this speed leading to an overall correlation of ($r = 0.92$, $P < .001$) for the field walking test. The difference in pedometer steps compared with observed steps (digital hand counter) was statistically significant at 40 m/min ($P < .001$). The RT3 does not count steps and therefore was excluded from this analysis (Fig. 1).

6MWT Data

The correlation of steps counted by digital hand counter was significant for both accelerometer detected step count (observed vs. detected steps: $r = 0.99$, $P < .001$), as well as pedometer-based step count (observed vs. detected: $r = 0.94$, $P < .001$). All mean values for 6MWT test data, including distance (m), steps, and activity counts (VMU), are depicted in Table 2. Group differences (NYHA I vs. NYHA II vs. NYHA III) were statistically significant for all investigated parameters except for RT3 VMU in NYHA I vs. NYHA II.

There was a tight correlation of 6MWT distance to RT3 vector magnitude (test 1: $r = 0.91$, $P < .001$ for both) (Fig 2), followed by a slightly weaker correlation of 6MWT distance to APM-detected steps (Test 1: $r = 0.87$, $P < .001$) (Fig 3). The correlation of RT3 activity counts (VMU) to APM detected steps was also strong ($r = 0.80$, $P < .001$), indicating that both parameters are equally valid. Repeated measures analysis of variance revealed no significant differences between 2 administrations of the 6MWT in any of the investigated parameters. The reproducibility of test results was within 95% margin for all 6MWT performance parameters including distance, step count, and RT3 VMU (Fig 4, Fig 5). Correlation strength with 6MWT distance was identical for test 2 ($n = 45$). All patients reached slightly greater 6MWT parameters in Test 2 (~3%), suggesting that practice does play a role in test outcome. Mean bias ± 95% confidence interval for test difference ($6MWT_1 - 6MWT_2$) of all investigated parameters are listed in Table 3.

Discussion

The main finding of this study is that accelerometers provide new data on walking performance during the 6MWT that might aid in future assessment of patients' exercise capacity. We could establish a good correlation between accelerometer-based step frequency, activity counts, and 6MWT distance, a well-established prognostic parameter particularly in terms of short-term prognosis. The accuracy with which accelerometers are able to detect physical activity in CHF patients suggests their clinical applicability in telemedicine by facilitating routine performance testing in form of a 6MWT in outpatient or home-based settings. This would allow for continuous patient monitoring over a given time frame and potentially assist in detecting a clinical regression in patients with advanced heart failure from a worsening of functional exercise capacity.

The high reproducibility in test results allows us to conclude that accelerometers offer reliable performance

Table 1. Clinical Characteristics of Study Population

	NYHA I	NYHA II	NYHA III	TOTAL	*P* Value*
n	12	19	19	50	
Gender men	8 (66%)	16 (84%)	14 (74%)	38 (76%)	.20
Women	4 (33%)	3 (16%)	5 (26%)	12 (24%)	
Age	69.9 ± 4.9†	58.1 ± 15.1	58.1 ± 14.8‡	60.9 ± 14.0	<.05
Height (cm)	170.3 ± 8.3	172.9 ± 8.3	170.0 ± 9.6	171.5 ± 8.8	.72
Weight (kg)	78.8 ± 19.0	85.1 ± 12.0	84.8 ± 17.5	83.5 ± 15.9	.85
VO_2peak (mL·kg·min)	26.6 ± 4.1§	23.1 ± 6.2‖	14.1 ± 2.8‡	20.5 ± 6.9‡	<.01
EF %	53.4 ± 7.6†	37.1 ± 15.2¶	33.2 ± 14.6‡	39.0 ± 15.5	<.01
LV diameter (mm)	55.5 ± 6.2§	64.2 ± 11.5¶	70.5 ± 11.0‡	63.4 ± 12.3	<.01
Diagnosis, HFPEF	7 (58%)	0 (0%)	0 (0%)	7 (14%)	<.01
Diagnosis, HFREF	5 (42%)	19 (100%)	19 (100%)	10 (86%)	<.01

NYHA, New York Heart Association; SD, standard deviation; LV, left ventricular function (diastolic); EF, ejection fraction; HFPEF, heart failure with preserved EF; HFREF, heart failure with reduced EF; VO_2peak, cardiopulmonary exercise testing.

Data are presented in means ± SD.

*Overall group comparison by analysis of variance; post hoc group differences were tested by *t*-test with: $P < .05$.

§NYHA I vs. NYHA II.

¶NYHA II vs. NYHA III.

†NYHA I vs. NYHA II; $P < .005$.

‖NYHA II vs. NYHA III; $P < .005$.

‡NYHA III vs. NYHA I; $P < .005$.

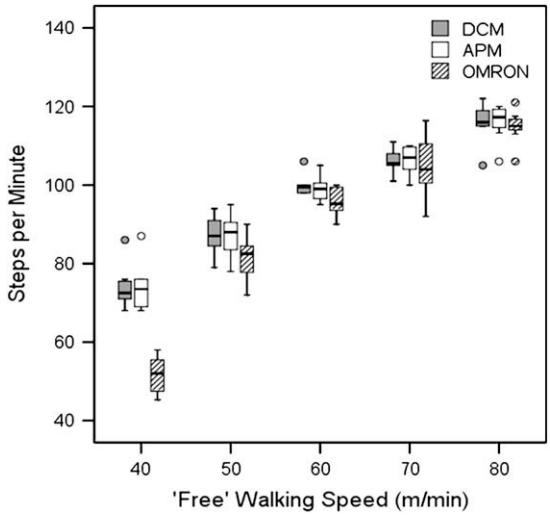

Fig. 1. Comparison of mean step count of DHC, APM, and OMRON in the field walking test. Comparison of mean step count of DHC (digital hand counter; gray boxes), APM (accelerometer; white boxes), and OMRON (pedometer; striped boxes) at different walking speeds during the field test. Steps per minute are averaged over 6-minute intervals. The circles represent outliers (values between 1.5 and 3 box lengths from the upper or lower edge of the box).

measures during a standardized exercise test that can be used alternatively to 6MWT distance. Several studies have used accelerometers, including pedometers, to quantify activity levels in CHF patients under free-living conditions,[4,17,18] but few have quantified accelerometer readings during a standardized exercise test and established significant correlation with an important prognostic parameter such 6MWT distance. Steele and colleagues investigated the Titrac R3D, a precursor model to the RT3, under free-living conditions and during the 6MWT in chronic obstructive pulmonary disease patients and found that accelerometer output, in terms of VMU, showed a tight linear correlation with 6MWT distance even after repeated measurements, indicating that results were highly reproducible.[19] Our study is the first, however, to analyze the use of step frequency to quantify physical performance during the 6MWT. Our findings demonstrate that this seems to be an additionally useful performance parameter to assess functional exercise capacity in CHF patients.

In this study, we explored different ranges of walking speed typically seen in CHF patients and evaluated how well the 3-dimensional accelerometer was able to detect steps compared to the 1-dimensional pedometer. Our results demonstrate that the accelerometer is accurate at detecting steps even during slow, irregular walking movements (≤40 m/min), which is typical for elderly patients with CHF. In contrast, the pedometer was less accurate in the low-intensity walking range. Similar results were previously reported by Le Masurier et al, who also found increasing detection error in pedometer readings with decreasing treadmill speeds (≤50 m/min) as opposed to accelerometer output.[20] Cytaro et al investigated pedometer reliability in elderly nursing home residents under free-living conditions and also found that pedometers were not reliable in accurately measuring step count in this patient population.[21] Therefore, the pedometer does not prove to be a suitable physical activity monitoring device in the sick or the elderly, but finds its applicability in healthy individuals with normal activity levels and walking speeds faster than 60 m/min.[15,22,23]

Gait analysis has shown that patients with CHF adjust their step frequency according to their self-selected walking speed, whereas their stride length remains roughly the same regardless of walking speed.[24,25] Patients with functional limitations hereby optimize their gait economics keeping energy requirements to a minimum.[4] The low variability in stride length with changing walking speeds further strengthens the use of step frequency as a suitable indicator of physical performance in this patient population.

As expected, step frequency increased proportionally to walking speed and 6MWT distance in the highs (≥600 m) and lows (≤400 m); however, overlapping 6MWT step counts were also seen in individuals with moderate 6 MWT distances (≥400 m ≤ 600 m), prohibiting a clear separation of these patients into their distinct NYHA functional class. Despite overall group differences being statistically significant, only NYHA I and III patients could clearly be distinguished based on individual 6MWT step counts. Nevertheless, the critical cutoff value when associating 6MWT distance with poor clinical prognosis

Table 2. 6MWT Performance Parameters First Test (n = 50)

	NYHA I	NYHA II	NYHA III	Total	P Value*
n	12	19	19	50	
6MWT distance (m)	633 ± 60.4†	555 ± 76.6‡	387 ± 93.3§	510 ± 129	<.001
Total 6 MWT step count (APM)	834 ± 62.5‖	734 ± 65.2‡	624 ± 114§	716 ± 119	<.001
Total 6MWT step count (Omron)	849 ± 38.4†	755 ± 67.8‡	598 ± 168§	717 ± 151	<.001
Total 6MWT activity counts (RT3)	14,577 ± 2852	12,996 ± 3307‡	7722 ± 2843§	11,338 ± 4195	<.001

NYHA, New York Heart Association; 6MWT, 6-minute walk test.
*Overall group comparison by analysis of variance; post hoc group differences were tested by t-test with: $P < .05$.
†NYHA I vs. NYHA II.
‖NYHA I vs. NYHA II; $P < .005$.
‡NYHA II vs. NYHA III; $P < .005$.
§NYHA III vs. NYHA I; $P < .005$.

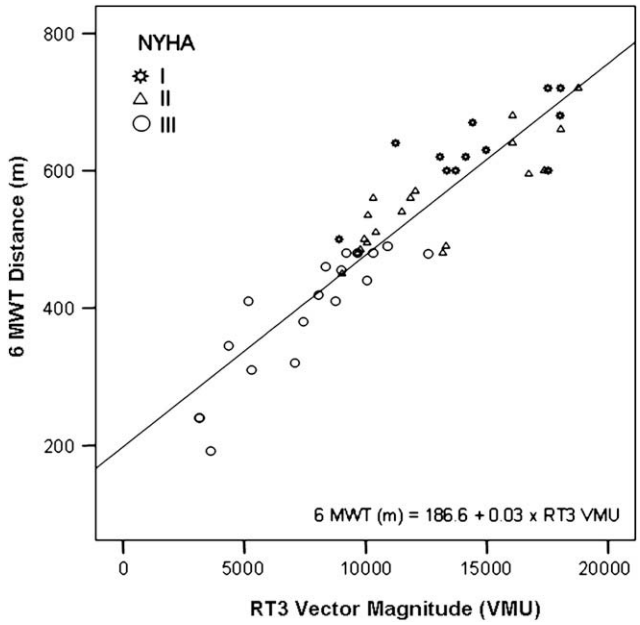

Fig. 2. Correlation of 6MWT distance (meters) and activity counts (RT3). Correlation of 6MWT distance (meters) and total 6MWT activity counts (RT3) with r^2 = 0.83, defined according to NYHA functional class (☼ = NYHA I), (△ = NYHA II), and (○ = NYHA III). 6MWT, 6-minute walk test; NYHA, New York Heart Association; VMU, vector magnitude units.

is ≤400 m.[13] Therefore, our data suggest that 6MWT step count has sufficient potential to identify patients with advanced stages of HF.

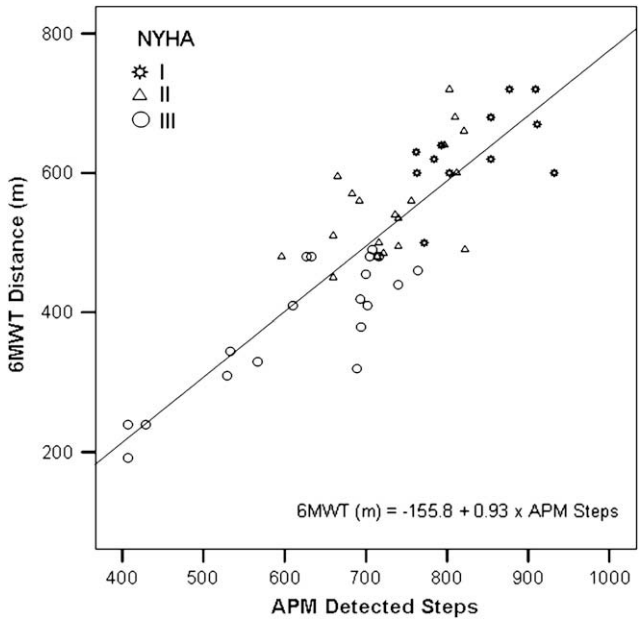

Fig. 3. Correlation of 6MWT distance and step frequency (APM). Correlation of 6MWT distance (meters) and total 6MWT step count (APM) with r^2 = 0.76, defined according to NYHA functional class (☼ = NYHA I), (△ = NYHA II), and (○ = NYHA III). 6MWT, 6-minute walk test; NYHA, New York Heart Association.

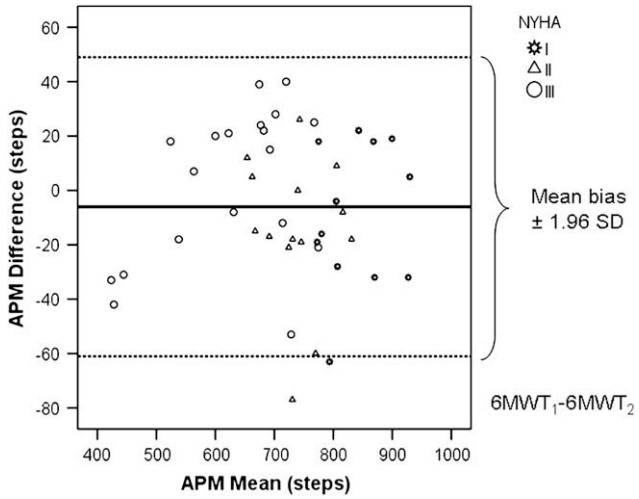

Fig. 4. Bland-Altman plot of 6MWT difference ($6MWT_1$ − $6MWT_2$) in total steps (APM) as a function of their mean (☼ = NYHA I), (△ = NYHA II), and (○ = NYHA III). 6MWT, 6-minute walk test; NYHA, New York Heart Association.

The RT3 has been thoroughly investigated and extensively evaluated under laboratory controlled and free-living conditions.[23,26,27] A recent study by Hussey et al compared RT3 output to indirect calorimetry measurements and found the device to provide valid estimates of inactivity, walking, and running at defined treadmill speeds.[28] A study by Rowlands et al showed that RT3 vector magnitude maintained a linear relationship with speed even at low- and high-intensity walking/running, whereas 1-dimensional accelerometers, including a pedometer, underestimated high-intensity as well as low-intensity activities.[29]

Defined vector magnitude cutoff points to differentiate sedentary, light, moderate, and vigorous activities have

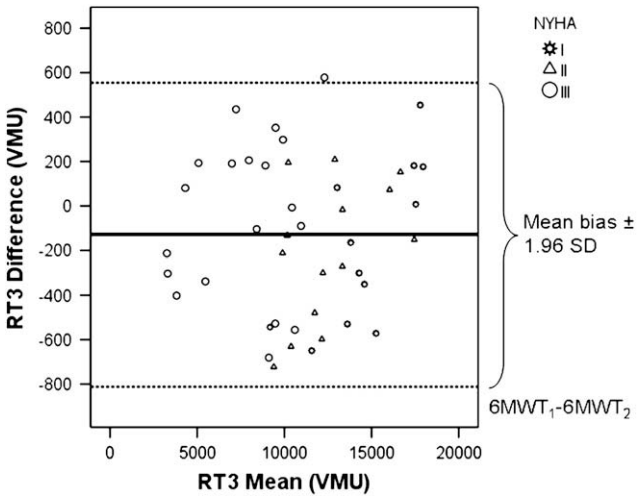

Fig. 5. Bland-Altman plot of 6MWT difference ($6MWT_1$ − $6MWT_2$) in total vector magnitude units (RT3) as a function of their mean (☼ = NYHA I), (△ = NYHA II), and (○ = NYHA III). 6MWT, 6-minute walk test; NYHA, New York Heart Association.

Table 3. Responses to 2 Consecutive 6MWTs ($n = 45$)

6MWT Variables			
	Test 1	Test 2	Mean Difference
Distance walked (m)	510 ± 129	516 ± 126	−6 ± 20
Total steps (APM)	716 ± 119	721 ± 121	−6 ± 27
Total steps (Omron)	717 ± 151	710 ± 138	−4 ± 61
Total VMU (RT3)	11,338 ± 4195	11,540 ± 4099	−129 ± 348

6MWT, 6-minute walk test; SD, standard deviation.
Values are expressed as the mean ± SD.

been previously reported by Treuth and colleagues to predict MET scores from accelerometer counts.[30] Despite our in-depth literature review, however, most studies we found regarding RT3 validity used adolescent, healthy individuals. Nguyen and colleagues investigated the RT3 in terms of physical activity measurements in chronic obstructive pulmonary patients and found that the device needed further validation work in terms of its physical activity output in a patient population with functional limitations similar to those seen in CHF.[31] As opposed to the study by Steele et al, their investigations were not based on evaluating accelerometer readings during a standard exercise test.

In this present study, we found the RT3 VM (the sum of movement velocity in the x, y, and z plane) to increase linearly with walking speed and step count. Although, similar to with 6MWT step count, we could find overlapping vector magnitude values for moderate 6MWT distances, it was less pronounced. Its linear association was further emphasized by the tight correlation of RT3 vector magnitude to 6MWT distance.

In terms of executing this approach, patients must be schooled on how to self-administer the 6MWT and a staff-supervised first test will be necessary to serve as reference for all consecutive testing. To ensure validity of test results, it is also important that patients perform all tests using the same test course. Exercise testing in form of a home- based 6WMT may require a more complex monitoring system of CHF patients including direct contact with the telemonitoring center at test begin, patient clearance to initiate 6MWT based on previous monitoring results, continuous electrocardiogram monitoring during testing, and, preferably, an accompanying person. This is being practiced in an ongoing pilot study (TIM-HF Studie NCT 00543881, www.clinicaltrials.gov). Future experience will show to which extent precautions are mandatory, because the likelihood of clinically relevant symptoms, significant changes on the ST-segment or complex ventricular arrhythmias during a 6MWT has been found to be very low.[32]

There are several limitations to this study. First, we did not account for age or gender in our study analysis. It must be pointed out that the influence of age and gender on the measurement of functional capacity with these devises has not been investigated and requires further investigation with a larger study population. In addition, the heterogeneity in our study population regarding heart failure etiology poses as a further limitation. Seven of 12 NYHA I patients had HF from ischemic heart disease with a preserved ejection fraction. Although clinical features in HF patients are similar, patients with HF and preserved ejection fraction tend to have a slightly better functional capacity compared with patients with HF and systolic dysfunction.[20] Thus it is possible that this difference it etiology accounts for some of the differences found among NYHA classes. However, the discrimination between NYHA II and III, which seems to be of strongest clinical importance, is probably not affected by this bias.

The cardinal prerequisite for using telemedical activity monitoring in patients with CHF is its simplicity and practicability under every day circumstances. On this basis, short-term physical activity monitoring by means of accelerometer would make routine performance testing in form of a 6MWT possible and, more specifically, would allow for significant decreases in exercise capacity to be recognized in time. A long-term study with a larger study population is needed, however, to validate the clinical applicability of the investigated parameters. In addition, these devises will have to be tested in a variety of clinical scenarios to determine if telemonitoring at home will indeed have the prognostic and clinical values suggested in this study.

Acknowledgment

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Pedometer Accuracy in Patients with Chronic Heart Failure

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Key words
- activity monitoring
- accelerometer
- 6-minute walk test
- step detection

Abstract

This study assesses the accuracy of the Omron HJ-720ITC pedometer at low walking intensities in patients with chronic heart failure. Step accuracy was assessed by visual observation on the treadmill and during free walking at 40, 50, 60, 70, 80 m/min, as well as during self paced walking using the 6 min walk test. A total of ninety-seven patients with heart failure (mean age: 61 ± 13, NYHA I, N = 30; NYHA II, N = 32; NYHA III, N = 35) participated in the study. At predefined walking speeds, a statistically significant % error in pedometer accuracy was evident at 60 m/min ($p = 0.039$), and % error increased markedly below this threshold. Highest % error in pedometer accuracy was seen at 40 m/min (mean bias (% error): 28.3 ± 9.0%; 95% CI: 21.8–34.7; $p < 0.001$). During self paced walking (6MWT) the absolute % error in pedometer readings was largest in patients with strongest functional limitations and 6 MWT distances < 400 m (mean bias (% error): 10.7 ± 13.6%; CI 5.6–15.4, $p < 0.001$). The Omron HJ-720ITC pedometer is accurate for monitoring activity in individuals with normal walking behaviour, but seems unsuitable for chronically ill patients characterised by slow walking gaits.

Introduction

The importance in monitoring ambulatory physical activity lies predominately in prevention and rehabilitation. This includes people with chronic diseases such as obesity, diabetes or heart failure and/or frail adults such as the elderly or otherwise functionally impaired. These individuals often present with slow and irregular walking gaits. Several previous studies investigating pedometer accuracy have reported increased detection error in pedometer readings with decreasing walking speeds (≤ 67 m/m) [1, 6, 11, 13, 15, 19–21]. In addition, associated gait disorders typically seen in elderly and/or chronically ill patients with functional limitations, greatly compromise pedometer accuracy [7, 17]. Cytaro and colleagues reported inadequate pedometer accuracy in elderly nursing home residents under controlled and free living conditions and concluded them unsuitable for monitoring ambulatory activity in these individuals [5].

Recently, a new generation of piezoelectric pedometers has emerged to abate the inaccuracy in step detection at slow walking speeds seen in the preceding pendulum technology. These pedometers show improved step accuracy at slower walking speeds irrespective of pedometer tilt angle and overall body placement. This is of particular importance when using pedometers in weight loss programs in overweight and obese individuals [4, 10, 12].

Nevertheless, slow walking speeds addressed in these studies markedly exceed habitual walking speeds of many individuals suffering from chronic diseases and functional impairments [1]. These individuals typically present with habitual walking speeds as low as 40 m/min. To this date, it has not been established if the accuracy of piezoelectric pedometers holds true for slow walking intensities in persons with chronic diseases. This needs to be addressed in order to examine if pedometers can be trusted to adequately measure activity levels in patients characterized by varying degrees of functional limitations. For this purpose, we explored the accuracy of a piezoelectric pedometer (HJ-720ITC by Omron) at walking speeds ranging from very slow to medium slow under controlled and non controlled walking scenarios in patients with chronic heart failure. This will help determine if such a device is suitable for monitoring ambulatory activity in

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the chronically ill or if its applicability is predominantly restricted to healthy individuals with normal activity levels.

Methods

Patient recruitment

Subjects were recruited at the heart failure outpatient clinic of a university hospital (phase IV patients) and in a rehabilitation clinic (in hospital phase III patients). Inclusion criteria were mild to moderate stable heart failure defined by New York Heart Association (NYHA) class I–III, regardless of age and medical history, and the willingness to participate in walking tests. Exclusion criteria were any unstable medical conditions that were contraindicative to exercise testing or if patients were unable to walk without assistance. The study complies with the Declaration of Helsinki and was approved by the university's ethics committee. This study has been performed in accordance with the ethical standards of the International Journal of Sports Medicine [8]. All patients signed an informed consent. A total of 113 CHF patients were screened and 97 patients eventually assigned to participate due to in/exclusion criteria. NYHA functional class was assigned by the treating physician based on clinical parameters, self perceived and maximal exercise tolerance. All patients included in the study had recently received a full cardiac checkup by their treating physician including an echocardiogram and exercise tolerance test within 4 weeks prior to study testing. Left ventricular ejection fraction (LVEF%) and peak oxygen uptake (VO_{2peak}) were adopted and are listed under baseline characteristics in ○ **Table 1**. All exercise tests conducted for this study were administered on different days.

Exercise testing

Controlled conditions

Treadmill Walking. A total of 10 NYHA I patients were randomly selected from the patient pool in order to test pedometer accuracy under controlled conditions. Patients were first asked to walk on the treadmill at 40, 50, 60, 70 and 80 m/min for 6 min per stage. The piezoelectric pedometer (OMRON, HJ-720ITC) was attached to a belt and positioned over the right hip. An assistant unaware of the purpose of the study, i.e. controlling pedometer accuracy at different walking speeds in patients with heart failure, counted steps manually by digital hand counter (HC-1, Voltcraft, Hirschau, Germany) as reference for step accuracy. Pedometer readings and steps counted were recorded after each elapsed minute and later compared. This provided six separate pedometer readings (steps/minute) per walking speed for each participant.

'Free' Walking. The same testing procedure as described during treadmill walking was repeated outside on a paved test course 100 m in length. The test course was marked every 5 m and walking speed was administered by an acoustical timing device. Subjects started at 40 m/min and were instructed to adapt their gait according to the sounding of the acoustical signal by ensuring they had covered 5 m between two given sound signals. After six minutes at each walking speed the length between each acoustical signal decreased to indicate an increase in walking speed until 80 m/min was reached. Steps were again counted manually by the same assistant as during the treadmill test and pedometer readings were recorded every minute.

Self paced walking

To test the device's accuracy under self paced walking conditions, all 97 patients recruited were asked to perform a 6 min walk test (6MWT). The 6MWT was conducted in an enclosed corridor on a measured course that was 40 m long. The course was marked every 5 m, and subjects were instructed to walk from one end to the other end, covering as much distance as possible during the six minutes. Subjects were allowed to rest if needed and remaining time was called every minute. The pedometer was attached in exactly the same fashion as previously described. Again steps were counted by digital hand counter as reference for step frequency and 6MWT distance was recorded upon test completion. The same assistant from the calibration test also counted steps during the 6MWT. Subjects were instructed to stand still after final time was called and steps measured by pedometer were recorded immediately.

Data analysis

Statistical analysis was done using PASW software (version 17.0, SPSS Inc.).

Data were descriptively analysed reporting mean ± standard deviation (SD) for quantitative measurements. Bivariate correlations of continuous variables were investigated using Pearson correlation coefficient (r). Box plots and scatter charts were provided to illustrate and quantify correlations of relevant measurements. Mean difference in pedometer steps versus actual steps was computed by pedometer steps – actual steps. To calculate the % error in pedometer steps versus actual steps we used the sample means of percent differences between actual steps and pedometer steps (100 × (pedometer steps – actual steps)/actual steps). Statistical significance of inaccuracy (bias reported as % error) in pedometer steps at defined walking speeds and during the 6MWT was assessed by two-way analysis of variance for repeated measurements including walking speed and measurement device as factor variables. In case of a significant global test for device, post-hoc pair wise group comparisons and Bonferroni correction of p-val-

Table 1 Baseline characteristics of study population.

	NYHA I	NYHA II	NYHA III	TOTAL	p-value#
N	30	32	35	97	
age	67.6 ± 9.0*	58.2 ± 14.1	57.1 ± 13.9†	60.7 ± 13.4	0.002
female	6 (20%)	6 (19%)	11 (31%)	23 (23%)	0.062
BMI (kg/m^2)	27.3 ± 4.0	27.9 ± 3.5	27.9 ± 4.8	27.7 ± 4.2	0.86
VO_{2peak} (ml/kg*min)	25.4 ± 4.1*	22.6 ± 5.5◆	14.1 ± 3.0†	20.7 ± 6.5	< 0.001
LVEF %	57.2 ± 12.2*	38.3 ± 15.4◆	30.5 ± 13.1†	40.1 ± 17.5	< 0.001

Data is presented in means ± SD; SD = standard deviation; BMI = body mass index; VO_{2peak} = maximum oxygen uptake; LVEF = left ventricular ejection fraction; # overall group comparison by ANOVA/Chi^2 test; post hoc group differences with $p < 0.05$: * NYHA I vs. NYHA II; ◆ NYHA II vs. NYHA III; † NYHA III vs. NYHA I

ues were conducted. Further, the corresponding 95% confidence intervals of mean% error were reported. To account for multiple comparisons, differences between peak NYHA groups were assessed by analysis of variance (ANOVA) followed by unpaired Student's *t*-test in terms of a hierarchical test procedure. The Chi^2-test was used to compare frequencies between independent samples. A two-sided p-value less 0.05 was considered to indicate statistical significance in all statistical analyses.

Results

Patient characteristics

Overall, a total of 97 patients (mean age: 60.7±13.4) with mild to moderate heart failure participated in the study (NYHA I, N=30; NYHA II, N=32; NYHA III, N=35) (**Table 1**). Of this entire patient pool, 10 NYHA I patients were randomly selected to complete the treadmill and 'free' walking calibration tests (**Table 2**), whereas all 97 patients were asked to perform the 6MWT.

Controlled conditions during treadmill walking

The overall correlation of pedometer steps and actual steps was good for the treadmill test (r=0.80, p<0.001), however high deviations between pedometer steps and actual steps were seen in the very slow walking ranges (40 and 50 m/min) in patients with heart failure (**Fig. 1**). A statistically significant mean difference and% error in pedometer steps versus actual steps was seen starting at 60 m/min (mean difference: 5.1±4.9 steps, p=0.039; mean bias (% error): 5.0±4.9%; 95%CI: 1.5–8.5). Pedometer accuracy decreased significantly at walking speeds below 60 m/min, reaching the highest detection error at 40 m/min (mean difference: 21.1±7.7 steps, p<0.001; mean bias (% error): 28.3±9.0%; 95%CI 21.8–34.7) (**Table 3**). Detailed distributions of % errors in pedometer reading at defined walking speeds during treadmill walking are illustrated in **Fig. 1**.

Controlled conditions during 'Free' walking

Similar observations to those in treadmill walking were made during the 'free' walking at predefined walking speeds. The overall correlation of pedometer steps versus actual steps was slightly higher during 'free' walking than during treadmill walking (r=0.86, p<0.001), however, similar high deviations in pedometer readings were observed in the low intensity walking range (40, 50, and 60 m/min) (**Fig. 2**). Similar to the treadmill test, a statistically significance difference in pedometer steps versus actual steps was apparent starting at 60 m/min (mean difference: 4.2±1.5 steps, p<0.001; mean bias (% error): 4.7±1.9%; 95%CI: 3.4–6.1) (**Table 3**). Again, the highest % error in pedometer readings was seen at 40 m/min (mean difference 17.7±7.4 steps, p< 0.001; mean bias (% error): 25.6±10.8%; 95%CI 17.9–33.3). Detailed distributions of % errors in pedometer reading at defined walking speeds during treadmill walking are illustrated in **Fig. 2**.

Table 2 Characteristics of patients participating in calibration tests.

	NYHA I
N	10
gender men	6 (60%)
women	4 (40%)
age	69.9±4.9**
height (cm)	170.3±8.3
weight (kg)	78.8±19.0
BMI (kg/m²)	26.9±2.3
VO_{2peak} (ml/kg*min)	26.6±4.1*

Characteristics of patients (NYHA I, N=10) participating in calibration tests treadmill walking and 'free' walking at predefined walking speeds to test pedometer accuracy under controlled conditions. Data is presented in means±SD; SD=standard deviation

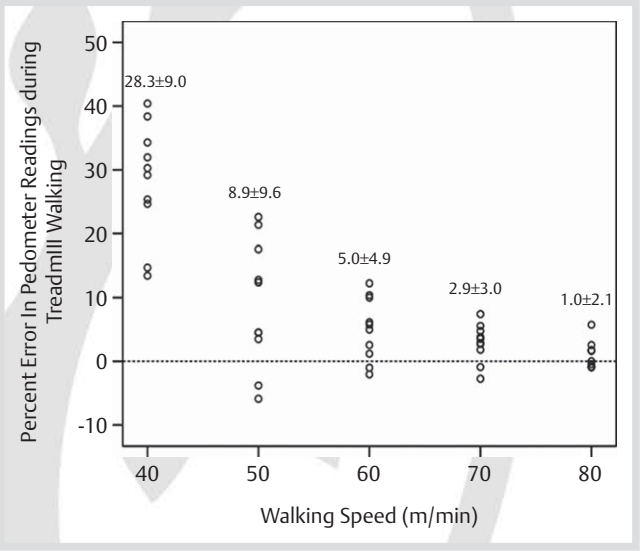

Fig. 1 Scatter plot of % error in pedometer steps vs. actual steps at defined walking speeds on the treadmill. Mean bias (% error) is calculated by taking: 100*(actual steps-pedometer steps)/actual steps. The dashed line represents 0% error in pedometer readings at defined walking speed. Mean values for % error at each walking speed are illustrated above each column.

Table 3 Steps and mean percent error (%) in pedometer steps versus actual steps at predefined walking speeds.

	Treadmill Walking			'Free' Walking		
Walking Speed	Mean Difference	p-value §*	Mean % Error (95% CI)	Mean Difference	p-value §*	Mean % error (95% CI)
40 m/min	21.1±7.7	<0.001	28.3±9.0 (21.8–34.7)	17.7±7.4	<0.001	25.6±10.8 (17.9–33.3)
50 m/min	8.2±7.9	0.019	8.9±9.6 (1.8–16.1)	6.9±4.7	0.006	8.6±5.8 (4.5–12.9)
60 m/min	5.1± 4.9	0.039	5.0±4.9 (1.5–8.5)	4.2±1.5	<0.001	4.7±1.9 (3.4–6.1)
70 m/min	3.1±3.2	0.066	2.9±3.0 (0.8–5.0)	2.3±2.6	0.134	2.3±2.8 (0.3–4.3)
80 m/min	1.3±2.5	0.763	1.0±2.1 (−0.5–2.5)	1.2±2.0	0.482	1.1±1.8 (−0.2–2.4)

Mean difference (actual steps – pedometer steps) and mean percent error (100×(pedometer steps – actual steps)/actual steps) at predefined walking speeds on the treadmill and during 'free' walking (NYHA I, N=12). Data is presented in means±SD; SD=standard deviation; CI=confidence intervals.

two-way ANOVA for repeated measurements:

p-value (main effect: actual steps vs. pedometer): <0.001

§ p-value interaction (speed vs. device) : <0.001

* Bonferroni corrected p-values (correction factor 5)

Self paced walking

Mean values for distance covered (m) during the 6MWT, pedometer steps and counted steps (DHC) during the 6MWT are listed in **Table 4**. Average walking speeds of NYHA I, II, III patients in the 6 MWT were 107 ± 13.5 m/min, 88 ± 11.8 m/min and 63 ± 15.8 m/min, respectively. Overall correlation of pedometer steps and actual steps was good (r = 0.95; p < 0.001), however significant discrepancies in pedometer readings were again seen at slower walking speeds (**Fig. 3**). Mean difference and mean % error was largest in patients with greatest functional limitation (NYHA III) and 6 MWT distances <400 m (**Table 5**). In this subgroup mean difference and mean bias of % error in pedometer readings averaged 55.8 ± 61.9 and 10.7 ± 13.6%; CI 5.6–15.4, p < 0.001, respectively.

Discussion

The Omron HJ-720ITC pedometer showed good accuracy at 'normal' range walking intensities (70 and 80 m/min) in patients with chronic heart failure and step detection at this speed was within the 3% error margin allowed for pedometers by the Japa-

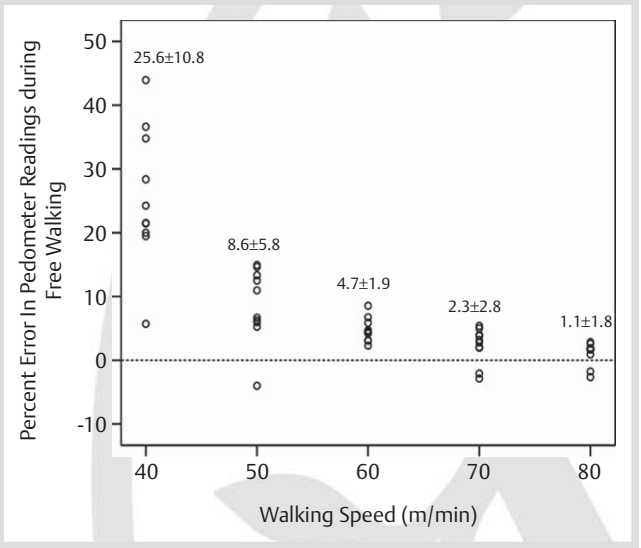

Fig. 2 Scatter plot of percent error in pedometer steps vs. actual steps at defined walking speeds during field testing. Mean bias (% error) is calculated by taking: 100*(actual steps-pedometer steps)/actual steps. The dashed line represents 0% error in pedometer readings at defined walking speed. Mean values for % error at each walking speed are illustrated above each column.

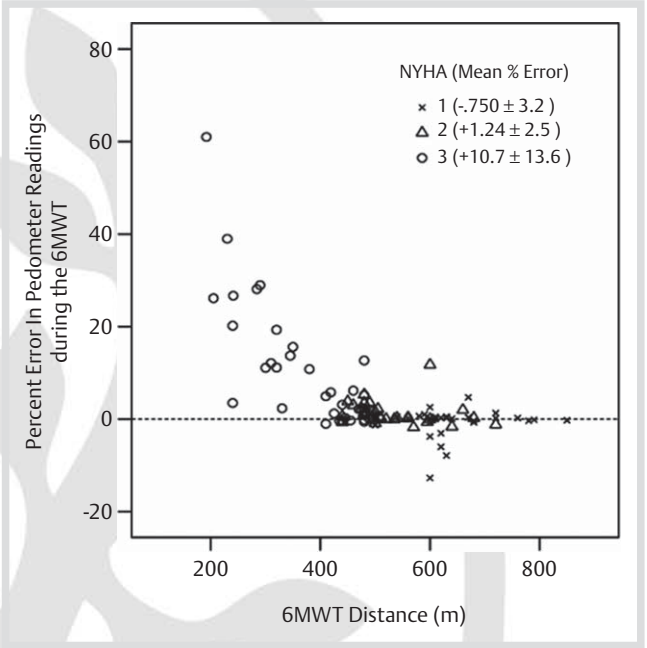

Fig. 3 Scatter plot of % error in pedometer steps vs. actual steps during the 6-minute walk test (6MWT). Mean bias (% error) is plotted against 6MWT distance (m) and patients are grouped according to functional limitations (NYHA class). NYHA I, N = 30 (crosses), NYHA II, N = 32 (triangles), NYHA III, N = 35 (circles). The dashed line represents 0% error in pedometer readings during the 6MWT.

Table 4 Results of the 6 min walk test (6MWT).

	NYHA I	NYHA II	NYHA III	TOTAL	p-value#
N	30	32	35	97	
6MWT Distance (m)	640 ± 81.2*	532 ± 70.9◆	378 ± 95.4†	510 ± 136	<0.001
6MWT Steps (DHC)	796 ± 64.2*	729 ± 71.0◆	614.7 ± 107†	708 ± 113	<0.001
6MWT Steps (Omron)	802 ± 62.9*	717 ± 68.7.0◆	559 ± 153†	686 ± 146	<0.001

Result of the 6MWT. Data is presented in means ± SD; SD = standard deviation; 6MWT = 6-min walk test; DHC = digital hand counter; Omron = pedometer
#overall group comparison by ANOVA/Chi² test; post hoc group differences with p < 0.05: * NYHA I vs. NYHA II; ◆ NYHA II vs. NYHA III; †NYHA III vs. NYHA I

NYHA Class	Mean Difference	p-value*	Mean % Error (95% CI)
NYHA I (N = 30)	−5.5 ± 25.5	0.25	− .750 ± 3.2 (−2.0–0.46)
NYHA II (N = 32)	9.4 ± 20.1	0.013	1.24 ± 2.5 (0.3–2.2)
NYHA III (N = 35)	55.8 ± 61.9	<0.001	10.7 ± 13.6 (5.6–15.4)
Total (N = 97)	21.5 ± 48.9	<0.001	4.0 ± 9.8 (2.0–6.0)

Table 5 Mean difference and mean percent error (%) in pedometer steps versus actual steps during the 6MWT.

Mean difference (actual steps – pedometer steps) and mean percent error.
(100 × (pedometer steps – actual steps)/actual steps) at self paced walking during the 6MWT according to the degree of functional limitation (NYHA class); Data is presented in means ± SD;
SD = standard deviation; CI = confidence intervals and statistical significance are based on t-test statistic
* Bonferroni corrected p-values (correction factor 5)

nese industrial standards. Nevertheless, it demonstrated a significant detection error below this threshold, reaching a maximum % error of almost 30% at walking speeds as low as 40 m/min. Similar observations were made during controlled (treadmill and 'free' walking) and self paced walking conditions. In the latter, the largest % error in step detection (>10%) was seen in individuals with greatest functional impairment (NYHA III) and 6 min walk distances <400 m/6 min. These findings greatly compromise the device's suitability to measure ambulatory activity in chronically ill individuals characterised by low walking intensities.

Our findings are in accordance with previous studies investigating the accuracy of piezoelectric pedometers at different walking intensities [18]. Karabulut and Crouter et al. examined the NL-2000 (New Lifestyles) piezoelectric pedometer at defined walking speeds in both healthy and obese individuals [4, 15]. In these studies, pedometer accuracy was also within the tolerated 3% error margin allowed by the Japanese industrial standards at 'normal' walking speeds (≥67 m/min), however, was greatly compromised below this threshold (67–54 m/min) by showing a significant increase in detection error (7–10%). Current studies by Holbrook and Hannson examine the validity and reliability of the piezoelectric HJ-151, HJ-112, and HJ-720ITC (Omron) in obese and non-obese individuals during treadmill and self paced walking conditions [10, 12]. They observed the devices to be highly accurate at step detection ranging from slow (67 m/min) to brisk walking speeds, regardless of pedometer body placement (hip, neck, chest pocket), and concluded them suitable for measuring ambulatory activity in obese individuals. Nevertheless, despite the accumulating evidence that piezoelectric pedometers are more accurate at slow walking speeds than spring levered pedometers, most studies have predominantly looked at healthy individuals with walking intensities in the moderately slow walking range (≥67 m/min).

Although previous studies have demonstrated augmented pedometer inaccuracy with decreasing walking speeds (Karabulut et al. went as low as 27 m/min) [4, 15, 18], our study is unique in having tested these devices in patients with chronic heart failure covering a spectrum of functional limitations. This is important as physical activity is closely linked to overall prognosis in various different chronic diseases [2, 3, 6, 9, 14, 22]. For this reason, means to objectively measure physical activity are rapidly gaining clinical interest. The findings of our study demonstrate a substantial error (>3%) in pedometer accuracy at low intensity walking speeds (60, 50, and 40 m/min) in patients with chronic heart failure. This is despite increased sensitivity of the piezoelectric technology. To exemplify the implication of our laboratory based findings into practical use, we investigated pedometer accuracy during a self paced walking test (6 min walk test), typically used in rehabilitation programmes. Here, too, detection error in pedometer readings increased at slow walking speeds similar to observations made under controlled conditions. Pedometer step accuracy was compromised the most in patients with greatest functional limitations (NYHA III) and 6 min walk distances below 400 m/6 min (or < 67 m/min). These patients often present with a discontinuous walking pattern (i.e. stopping and continuing, shuffling of feet), suggesting that detection error might become further exacerbated by the presence of an irregular walking pattern. This has previously been reported for pendulum pedometers [16, 17].

The divergence in findings regarding pedometer accuracy lies predominately in the type of pedometers used (piezoelectric versus pendulum technology), the walking intensities investigated, as well as the study population observed (healthy versus diseased and/or obese). The apparent fallacy of many studies lies in having investigated a young and seemingly healthy sample population and then extrapolating their results onto various populations characterized by a variety of diseases and limitations. Walking patterns of individuals with true functional limitations are unique and not naturally reproducible by healthy subjects. Thus, conclusions made based on general assumptions are questionable in terms of their validity. The strength of our study is that we used a chronically ill population with a spectrum of functional disabilities in order to derive our conclusions.

In summary, our findings illustrate that the HJ-720ITC piezoelectric pedometer is not suitable for measuring steps at low intensity walking speeds in patients with chronic heart failure. Therefore, although the use of pedometers is advantageous, their applicability seems restricted to healthy individuals at present. Pedometers are easy and inexpensive tools for monitoring physical activity in rehabilitation programs. However, more work is needed to utilize them in chronically ill patients characterized by low walking intensities.

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Association of Physical Activity and prognostic parameters in elderly patients with heart failure

Physical activity monitoring in CHF

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ABSTRACT

Objective: To evaluate three different methods for assessing free living physical activity (PA) in elderly patients with heart failure and how PA measurements are associated with established prognostic parameters.

Methods: The study included fifty patients with heart failure (NYHA I - III; mean age: 61.9 ± 4.0). PA measurements were assessed by questionnaire (AQ), pedometer and accelerometer. Seven days of PA were assessed and correlated with established prognostic parameters including VO_2peak, LVEF%, NTproBNP, and NYHA functional class.

Results: Accelerometry showed a slightly stronger correlation with VO_2peak and NYHA class (R = 0.73 and R = - 0.68; $P < 0.001$) than AQ (R = 0.58 and R = - 0.65; $P < 0.001$) or pedometer (R = 0.52 and R = - 0.50; $P < 0.001$). In addition, accelerometry was the only consistent independent predictor of VO_2peak in the multivariable regression model ($P = 0.002$), whereas AQ and pedometer were not independently associated with or predictive of VO_2peak ($P = 0.82$ and $P = 0.61$, respectively).

Conclusion: PA assessed by accelerometer is significantly associated with exercise capacity in patients with heart failure and is predictive of disease severity. PA monitoring can aid in evaluating clinical status.

Key Words: exercise rehabilitation; accelerometry; physical activity measurement; public health; chronic disease management;

INTRODUCTION

Daily activity levels are closely linked to exercise capacity and clinical prognosis in patients with heart failure (4;7;18;35). Therefore, measurement tools enabling the accurate assessment of daily activity are rapidly gaining in clinical importance (12;24;25).

The most common methods to measure physical activity include activity questionnaires and motion sensors, i.e. accelerometers or pedometers. Several studies have used these tools in the past to assess physical activity under controlled and free living conditions in various patient populations (19;23;27).

Activity questionnaires are able to cover a broad spectrum of activities, are fairly simple and cost-effective. However, they are easily biased by the subject's truthful rapport and are memory dependant which can be difficult especially in the elderly (30). Moreover, activity questionnaires primarily access purposeful movements in terms of exercise or transport and focus predominantly on activities with moderate to heavy intensities (22). Low intensity occupational or routine activities such as house hold chores, gardening, walking or standing are usually only superficially accounted for (16). Although questionnaires have been composed specifically for the elderly and patients with functional limitations (5;11), it is difficult to compose questions that are general enough to target a large group of people yet, at the same time, capture sufficient detail about ubiquitous, non specific activities (2;26).

Motion sensors such as pedometers and accelerometers allow for an objective measure of physical activity, however are limited to walking based movements. Pedometers are easy to use and are fairly low in cost, however have been shown to be unreliable at detecting steps during slow, irregular walking (8;17;21). Unlike pedometers, accelerometers can provide detailed information about exercise intensities and times spent in activity, but are expensive and require a computer for data analysis in addition to sufficient technical expertise (1).

The purpose of this study was to compare three different methods for measuring physical activity (PA) in a sample of elderly heart failure patients. We wanted to assess how PA measurements relate to established prognostic parameters (VO_2peak, LVEF%, NTproBNP, and NYHA class), and which PA measurement best predicts laboratory based exercise capacity (VO_2peak). This information will highlight the significance of measuring daily PA levels in patients with heart failure and suggest the best method for documenting PA in large epidemiological studies.

METHODS

Patient Recruitment

Fifty patients with heart failure were recruited with the cooperation of a heart failure outpatient clinic at the local university hospital and by advertisement in the local newspaper. The study complies with the Declaration of Helsinki and was approved by the local university's ethics committee. Inclusion criteria were mild to moderate stable systolic and/or diastolic heart failure defined by New York Heart Association (NYHA) class I – III (34), regardless of age and medical history, and willingness to participate in further clinical and laboratory analyses. Exclusion criteria were any unstable medical conditions that were contraindicative to exercise testing. 40% of heart failure patients participated in a cardiac rehabilitation program (1-2 times per week). Patients had a previous medical history at the heart failure outpatient clinic including diagnosis and treatment and were scheduled for their quarterly follow-up. Once included, patients signed an informed consent and were re-examined by two independent physicians. This included medical history, self perceived exercise tolerance, echocardiography, NTproBNP levels and cardio-pulmonary exercise testing, resulting in a NYHA classification of N = 12 NYHA I, N = 19 NYHA II and N = 19 NYHA III.

Echocardiography

Left ventricular remodelling including ejection fraction (%), systolic and diastolic LV chamber dimensions (LVEDD and LVESD) were assessed by two-dimensional echocardiography with the subjects in the left lateral decubitus position, according to the recommendation of the American Society of Echocardiography (28) and after at least 15 minutes of rest. A standardized imaging protocol was adopted with cross-sectional imaging of the left ventricle immediately distal to the mitral valve tips and apical two-dimensional

imaging based on orthogonal four-chamber views. M-mode measurements applied to leading edge principle as recommended by the American Society of Echocardiography (20). M-mode left ventricular ejection fraction based was equal to (EDV - ESV)/ EDV where the EDV = end diastolic volume and ESV = end-systolic volume.

Exercise Testing

Bicycle Ergometry: Following echocardiography, each subject undertook a symptom-limited cardiopulmonary exercise test (CPET) (fixed ramp protocol: start 10 watts; increase 10 watts/minute) using an electronically operated cycle ergometer (Sport Excalibur, Lode Medical technology, the Netherlands). This protocol was chosen based on the European recommendations for exercise testing in heart failure patients (36). The test was performed in the early afternoon under non-fasting conditions and subjects were encouraged to exercise to exhaustion or until signs of arrhythmias or ischemia developed. Maximal exertion was defined as meeting the following exhaustion criteria: 1) RER>1.0; 2) Borg ≥ 18; 3) pedaling frequency ≤ 60 rpm. Respiratory gases were analyzed via ZAN metabolic cart (ZAN 600 USB CPX, nSpire Health GmbH, Germany). VO_2 and VCO_2 were measured every 10s and peak oxygen consumption VO_2peak was defined as the highest oxygen consumption reached during cycle ergometry. Heart rate was measured on a 12-lead ECG and the electrocardiogram was monitored continuously. Blood pressure was measured at rest, in one minute intervals during exercise and during the recovery phase (5 min). Perceived exertion using the Borg scale was recorded at the end of each stage. Maximal heart rate (HR_{max}) was defined as the highest heart rate achieved during cycle ergometry.

6 Day PA Assessment

Patients were given an accelerometer (Aipermon® GmbH, Germany) and a pedometer (Omron HJ-720ITC) to wear at home to record their activity while going about there daily business. The accelerometer and pedometer were attached on the left and right hip, respectively, and patients were instructed to wear the devices consecutively for at least twelve hours a day for eight consecutive days (i.e. Monday through Monday). The motion sensors were to be attached upon rising in the morning and only to be dismounted for showering, bathing and sleeping. Since the first and last day (days on which devices were received and returned) were not complete days, these data were excluded from our analysis leaving 6 consecutive days of activity data (Tuesday – Sunday). Patients received the devices at random days of the week depending on their appointment for their base line visit. All device settings (date, time, weight, age and gender) were pre-programmed for each patient upon receiving the motion sensors thereby minimizing the patient's need to self handle the devices during the wearing period. Upon return, data from both devices were copied onto a PC, and its contents were viewed via customized computer programs (ActiCoach MPAT2Viewer, Aipermon® and OMRON Health Management Software). Daily physical activity measurements by pedometer were computed based on the total amounts of steps per day and accelerometer data was computed based on the total time (minutes per day) spent walking. Accelerometer detection accuracy has previously been extensively validated in patients with heart failure and detailed results are reported elsewhere (17). In summery, the device is able to accurately detect steps to 99% at walking speeds ranging as low as 20 m/min onwards. There is a 3 second detection delay in recognizing walking activity and initializing step count. We compared accelerometer detected steps with steps counted by digital hand counter and found a strong correlation between both measurements ($R = 0.99$, $P < 0.001$) with mean difference not statistical

significant with mean 0.1 ± 2.0 (p = 0.7). Similar good detection accuracy (pedometer vs. hand counted steps) was found for the Omron pedometer (R = 0.95, $P < 0.001$). Due to space limitation these data are not include in this study.

Activity Questionnaire (AQ):

Upon return, patients were asked to complete an activity questionnaire about their weekly activity (7 days) that has been validated in Germany particularly for the use of cardiac rehabilitation (10). It is composed of 13 main questions each containing one or more sub-questions (Table 2). 5 questions cover the weekly time spent doing occupational activities, daily household tasks, gardening and climbing stairs; 6 questions cover the weekly time exercising in terms of targeted sports (bowling, dancing, swimming, running etc), and two questions relate to weekly relaxation time and overall self perception of activity levels. Points are given depending on the time spent in each activity divided into 15, 30 and 60 minute time frames and according to the intensity with which this activity was performed, i.e 15 min of walking (0.7 points), brisk walking (1.3 points), running (1.9 points), 15 min of biking at 75 watt (1 point), 100 watt (1.4 points), 150 watt (2.5 points), 15 min of swimming (1.5 points). Points are summed up at the end of the questionnaire to give a total point score which is evaluated in terms of meeting certain activity requirements per week:

insufficient activity levels: < 14 points ≡ less than 1 hour/week or ≤ 500 kcal/week;

minimal activity requirements fulfilled: 15-29 points ≡ 1-2.5 hours/week or ≤ 1000 kcal/week; satisfactory activity levels: ≥ 30 points ≡ 3-4 hours/week or ≤ 2000 kcal/week;

high activity levels: ≥ 40 points ≡ >4 hours/week or > 2000 kcal/week;

Data Analysis

Statistical analysis was done using SPSS software (version 17.0, SPSS Inc.). Data were descriptively analysed reporting mean ± standard deviation (SD) for quantitative measurements and percentages for frequencies. Bivariate correlations of continuous variables were investigated using Pearson correlation coefficient (r). Scatter charts including linear regression lines as well regression equations were provided to illustrate and quantify correlations of relevant measurements. The Chi²-test was used to compare frequencies between independent samples. To account for multiple comparisons, differences between NYHA groups were assessed by analysis of variance (ANOVA). Therefore, in order to reduce the fraction of false positive results (significance by chance) a correction of *P*-values was necessary. In all data analyses *P*-values less than 0.05 were considered as statistically significant. Univariate and multivariable regression analyses were performed to test for which of the activity measurements were significantly associated with and independently predictive of VO_2peak. Test of variable interaction was confirmed by linear regression model. A discriminate analysis was performed to assess the accuracy of prediction of each PA measurement on correctly classifying patients into their assigned NYHA class.

RESULTS

Patient Characteristics

50 patients with heart failure (12 NYHA I, 19 NYHA II, 19 NYHA III) participated in the study. The mean age of all subjects was 61.9 years and 79% were men. Mean VO_2peak and ejection fraction (EF %) for NYHA I, II and III was 26.6, 23.1 and 14.1 ml/kg/min, and 53%, 37% and 33%, respectively. Most patients were taking ACE-inhibitor, beta-blockers, and diuretics (see Table 1 for detailed overview).

Physical Activity (PA) Measurements:

Mean values ± SD for PA measurements and corresponding group differences (*P*-values) are listed in Table 1. Question domains covered in the activity questionnaire (AQ) are listed in Table 2 (see Method section for how points are allocated). The activity questionnaire (AQ) was quantified according to a point scoring system, pedometer scores were quantified by means of total steps per day, and accelerometer scores were quantified according to time (min/day) spent doing walking activities. Mean pedometer and accelerometer wearing times were 13.02 ± 1.4 hours/day, 12.75 ± 1.4 hours/day and 12.51 ± 1.5 hours/day for NYHA I, II and III, respectively.

AQ correlated significantly with VO_2peak (R = 0.58; $P < 0.001$), LVEF (R = 0.49; $P < 0.001$), NTproBNP (R = 0.42; $P < 0.001$) and BMI (R = 0.31; $P = 0.03$). Likewise, accelerometer activity correlated significantly with VO_2peak (R = 0.73; $P < 0.001$), LVEF (R = 0.43; $P < 0.001$) and BMI (R = 0.35; $P = 0.01$), however not with NTproBNP (R = 0.26; $P = 0.073$). Meanwhile, pedometer activity only correlated significantly with VO_2peak (R = 0.55; $P < 0.001$) and BMI (R = 0.42; $P = 0.002$), but not with LVEF (R = 0.23; $P = 0.10$) or NTproBNP (R = 0.12; $P = 0.42$).

We performed a univariate regression analysis to assess which of the three activity measurements was predictive of VO_2peak without any additional influencing factors. AQ, pedometer and accelerometer scores were all significantly associated with VO_2peak when assessed independently ($P < 0.001$) (see Table 3). Subsequently, we performed a separate multivariable regression analysis for each activity measurement with VO_2peak as the dependent variable, each activity measurement as the independent variable, and BMI, Age, LVEF, and NTproBNP as influencing factors. Here too, the AQ score ($P = 0.03$), pedometer score ($P = 0.001$), and the accelerometer score ($P < 0.001$) were independently predictive of

VO_2peak despite the presence of additional influencing factors. When we added NYHA class as an additional influencing factor, however, only the accelerometer score remained independently predictive of VO_2peak ($P = 0.003$), while AQ and pedometer scores lost their significant association with VO_2peak ($P = 0.66$ and 0.09, respectively) (see Table 2). This is also illustrated in Figure 1 (AQ score) and Figure 2 (pedometer score) as the range of scatter for each of the activity measurements increases with increasing VO_2peak (decreasing NYHA class), whereas accelerometer scores stay fairly linear throughout all three NYHA classes (Figure 3).

When combining all independent co-factors into a multivariable regression model including all three PA measurements with VO_2peak as the dependent variable, and LVEF, BMI, NTproBNP, age, and NYHA class as influencing factors, only accelerometer activity remained independently associated with and predictive of VO_2peak ($B = 0.051 \pm 0.02$; $P = 0.014$), whereas pedometer and AQ scores did not ($P = 0.82$ and $P = 0.61$, respectively).

Finally, we performed a discriminate analysis to assess the accuracy of prediction of each PA measurement on correctly classifying patients into their assigned NYHA class (Table 4). Both the AQ and accelerometer score reached an overall correct classification of 60% (AQ: 67% NYHA I, 33% NYHA II, 80% NYHA III and 59% NYHA I, 22% NYHA II, 95% NYHA III). The pedometer score (steps/day) was weakest in correctly classifying patients into their assigned NYHA class with only 54% overall correct classification (42% NYHA I, 39% NYHA II, 75% NYHA III).

DISCUSSION

The results of this present study suggest that in patients with varying degrees of heart failure, daily activity measurements by means of accelerometer are more tightly associated with clinical prognosis (VO_2peak) than questionnaire or pedometer based measurements. This is supported by the strong correlation of accelerometer score with important prognostic parameters (VO_2peak, LVEF and NTproBNP) in addition to its significant and independent association with VO_2peak in the regression analyses. Although all three physical activity measurements were significantly associated with VO_2peak in the univariate analysis, accelerometer score was the only consistent independent predictor of VO_2peak when combining all factors associated with clinical prognosis (NYHA class) into a multivariable regression model. In addition, accelerometer score (walking min/day) showed the highest accuracy of prediction in patients with more severe heart failure by classifying 95% of NYHA III patients correctly into their assigned NYHA class. Overall correct classification incorporating the entire study population was identical between accelerometer and AQ score whereas the pedometer score (steps/day) showed the lowest accuracy of prediction overall.

These findings suggest a potential usefulness of activity monitoring by means of accelerometer in patients with varying disease severity as it might allow for identifying individuals with more advanced stages of heart failure. Timely detection of disease progression is critical in facilitating conventional therapy and guiding the rehabilitation progress in patients with heart failure.

Total activity assessed by activity questionnaire showed a moderate but significant correlation with prognostic parameters, however failed to be independently predictive of VO_2peak. This is most likely due to the fact that our study population consisted of individuals in which habitual activities such as daily walking predominate, however are difficult to recall

and may be underestimated. This is a limitation of recall questionnaires and supports the use of more objective measures of physical activity (1). Similar findings have been reported by fellow investigators showing a marked underestimation of questionnaire based activity measurements in the direct comparison of both methods (2;29). This is most likely due to the nature of the activity questionnaire as it is limited to measuring purposeful activity in terms of exercise or transport as opposed to ubiquitous movement associated with daily living (3;22).

In this present study mean age of NYHA I patients was past seventy years leading to the assumption that an underestimation of the activity questionnaire could be due to the poor recollection of the participants (13). However, difficulties in accurately recalling weekly activity from memory have also been observed in younger subjects indicating that memory skills are not entirely age dependant and that questionnaire outcome is not entirely memory dependant (9). Part of the problem lays in the difficulty to differentiate between recent versus habitual activity and underlines the fact that different activity dimensions are being measured in the activity questionnaire compared to motion sensors (23). Moreover, the actual performance and memory of a skill is dependent on the individual's perceived ability to accomplish that skill and its associated level of difficulty (11). This explains why most individuals without symptom limitations don't recall effortless, mundane activities, but focus their attention more towards vigorous activities in terms of exercise when completing a questionnaire.

Pedometer activity in terms of total steps per day also showed a moderate correlation with prognostic parameters, but was also unable to be independently predictive of VO_2peak. In addition it had the lowest predictive value in terms of identifying patients with more advanced heart failure (NYHA III) and overall. The bench mark of 3500-5000 steps per day has been set for sedentary individuals and/or persons with chronic diseases (31;32) and less

than 25000 steps per week has been associated with an increased mortality risk in patients with heart failure assessed by means of pedometer scores (35). Our participants all had step counts between 5000 – 9999 steps/day which is in the low active to somewhat active category (31). This might be partly be due to motivation of the participants (6) in addition to the improved technologies (pendulum vs. piezoelectric) pedometers are equipped with these days, allowing steps to be detected more precisely even at slow walking speeds (14;15). Considering the evidence suggesting that 30 minutes of minimally moderate walking translates into 3000 – 4000 steps (33), our subjects should have presented with even higher actual step counts when directly comparing the relationship between pedometer based steps/day and accelerometer based walking time/day in this study. The only explanation we have for this discrepancy is that participants moved at relatively slow walking speeds and that a significant portion of this walking time is accumulated by intermittent walking and standing as opposed to continuous walking.

There are several limitations to this study. The AQ based activity levels were computed by means of a cumulative weekly activity score, whereas both pedometer and accelerometer data were analyzed according to daily activity (steps /day or min/day). In addition, we only covered six days of activity with the motion sensors whereas the AQ was based on a typical seven day week. It seems unlikely that this incongruity in the number of assessment days greatly affected our data outcome as, however we can't exclude the possibility. Lastly, our study population was small and the cross-sectional study design limits any conclusions about the prognostic significance of our findings. Clearly, a longitudinal study with a larger patient group is required to validate these findings in order to better understand the association of daily activity and clinical prognosis especially in functionally stronger impaired stages of chronic heart failure.

In conclusion, accelerometer based activity measurements showed the strongest association with VO_2peak and other prognostic parameters when comparing three different methods for assessing physical activity levels in elderly individuals with heart failure. Our data suggest that accelerometer based PA measurement is indicative of overall exercise capacity and is able to discriminate patients with more advanced stages of heart failure. Not only targeted walking, but also ubiquitous walking associated with daily living play a contributing role in terms of clinical prognosis. In this regard, accelerometers allow for a more detailed analysis of activity. This should be taken into consideration when documenting PA in large epidemiological studies and/or monitoring patient progress in rehabilitation programs.

Conflict of Interest: None declared

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FIGURE LEGEND:

Figure 1. Correlation of Activity Questionnaire and VO_2peak

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of activity questionnaire (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 14.2 + 0.17 x AQ; (R = 0.57; $P < 0.001$).

Figure 2. **Correlation of Pedometer Score and VO_2peak**

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of pedometer (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 11.1 + 0.001 x steps; (R = 0.55; $P < 0.001$).

Figure 3. **Correlation of Accelerometer Score and VO_2peak**

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of accelerometer (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 8.9 + 0.098 x walking time; (R = 0.73; $P < 0.001$).

TABLES

Table 1: Patient Characteristics

	NYHA I	NYHA II	NYHA III	TOTAL	*P*-value[#]
N	12	19	19	50	
Gender Men Women	8 (66%) 4 (33%)	16 (84%) 3 (16%)	14 (74%) 5 (26%)	38 (76%) 12 (24%)	0.20
Age (years)	69.9 ± 4.9*	57.3 ± 5.1	58.9 ± 4.8†	61.9 ± 4.0	0.03
BMI (km/m^2)	26.8 ± 4.9	28.3 ± 3.4	29.4 ± 5.2	28.4 ± 4.5	0.32
VO_2peak (ml/kg*min)	27.6 ± 6.9*	23.0 ± 5.9$^{\blacklozenge}$	14.1 ± 2.8†	20.5 ± 7.5	<0.001
LVEF %	53.4 ± 7.6*	38.1 ± 13.2	31.5 ± 8.7†	39.6 ± 14.1	<0.001
NTproBNP (pg/ml)	2108 ± 1329	1365 ± 1074	569 ± 778†	1471 ± 1330	0.04
Pedometer (Steps/day)	9466 ± 3362	7795 ± 2726$^{\blacklozenge}$	5446 ± 2650††	7257 ± 3226	<0.001
Accelerometer (minutes/day)	167 ± 39.0	138 ± 57.6$^{\blacklozenge\blacklozenge}$	74.0 ± 21.3††	119 ± 56.6	<0.001
Questionnaire (point scoring system)	62.2 ± 30.1*	41.2 ± 17.7$^{\blacklozenge\blacklozenge}$	22.0 ± 12.1††	38.7 ± 24.9	<0.001
Medication					
ACE Inhibitor	6 (50%)	14 (74%)	15 (79%)	35 (70%)	
ARB	3 (25%)	4 (21%)	5 (26%)	12 (24%)	
Beta-Blocker	9 (75%)	17 (89%)	16 (84%)	44 (84%)	
Diuretics	7 (58%)	15 (79%)	19 (100%)	41 (82%)	

Table 1. Clinical characteristics of study population. Data is presented in means ± SD; SD = standard deviation; BMI = body mass index; VO_2peak = peak oxygen consumption; LVEF = left ventricular ejection fraction; [#]overall group comparison by ANOVA / Chi² test; post hoc group differences were tested by t-test with: p<0.05: * NYHA I vs. NYHA II; $^{\blacklozenge}$ NYHA II vs. NYHA III; † NYHA III vs. NYHA I;

Table 2: Activity Questionnaire

1. Levels of activity at work or in the home (minutes per day)
2. Amount of daily time spent walking to work or shopping (minutes per day)
3. Amount of daily time spent walking for leisure/exercise (minutes per day)
4. Amount of daily time spent riding a bike to work or shopping (minutes per day)
5. Amount of daily time spent riding a bike for leisure/exercise (minutes per day)
6. Amount of time spent gardening per week (hours per week)
7. Amount of flight of stairs climbed per day and how often (number of flights*frequency)
8. Weekly time spent going dancing or bowling (hours per week)
9. Amount of time spent swimming, walking, or jogging (hours per week)
10.Indicate weekly regular exercise (exercise type/frequency/duration)
11.Indicate total amount of regular exercise per week (minutes)
12. Indicate hours per day spent for relaxation
13. Indicate how you would view yourself in terms of your activity levels

Table 2: Questions included in the activity questionnaire

Table 3. Univariate and Multivariable Regression Analyses

	Univariate* Regression Analysis		Multivariable** Regression Analysis	
	B ± SE	*P*-value	B ± SE	*P*-value
AQ (activity points)	.17 ± .04	< .0001	.09 ± .04	.03
			.02 ± .04	.66§
Pedometer (steps/day)	.0001 ± .0001	< .0001	.001 ± .0001	.001
			.0001 ± .0001	.09§
Accelerometer (walking in min/day)	.01 ± .013	< .0001	.07 ± .014	< .0001
			.05 ± .016	.003§

*dependent variable is VO_2peak;
**multivariable analysis including BMI (kg/m^2), Age (years), LVEF (%) and NTproBNP (pg/ml);
§ multivariable analysis including BMI (kg/m^2), Age (years), LVEF (%), NTproBNP (pg/ml) and NYHA class;

Table 4. Discriminate Analysis (Test for Accuracy of Prediction)

Accuracy of Prediction (%)	NYHA I	NYHA II	NYHA III	Overall
AQ (points)	67%	33%	80%	60%
Pedometer (steps/day)	42%	39%	75%	54%
Accelerometer (walking min/day)	59%	22%	95%	60%

% correct classification of patients into the assigned NYHA class; each PA measurement is assessed separately;

Figure 1. Correlation of Activity Questionnaire and VO_2peak

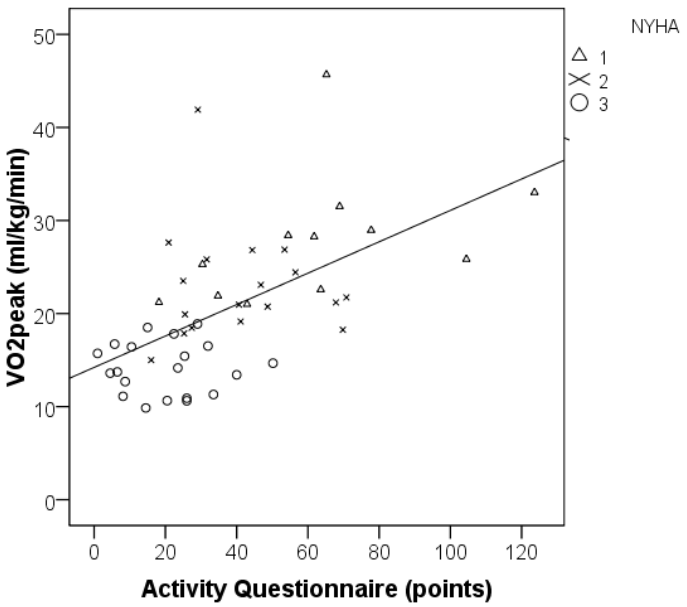

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of activity questionnaire (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 14.2 + 0.17 x AQ; (R = 0.57; $P < 0.001$).

Figure 2. Correlation of Pedometer Score and VO_2peak

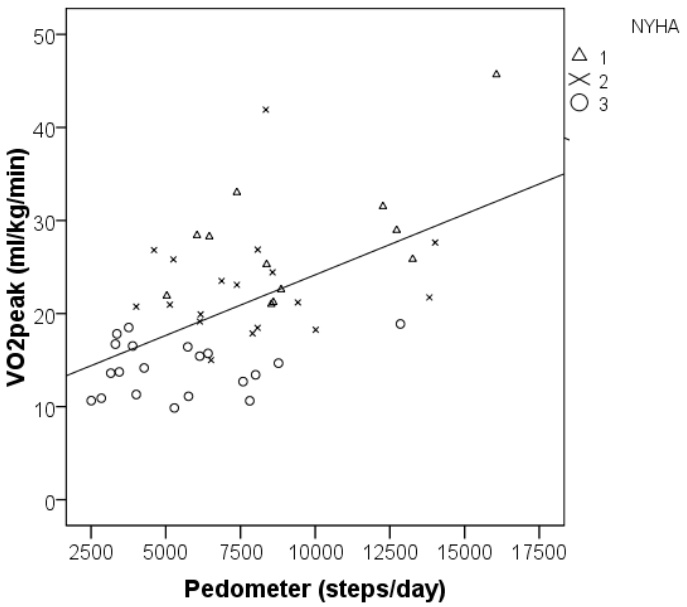

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of pedometer (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 11.1 + 0.001 x steps; (R = 0.55; $P < 0.001$).

Figure 3. Correlation of Accelerometer Score and VO_2peak

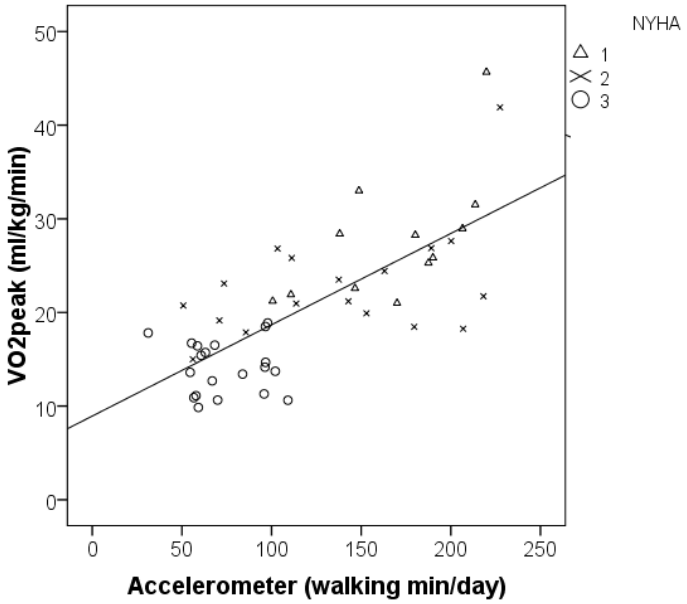

Figure Legend: Scatter plot showing the relation of VO_2peak and PA measured by means of accelerometer (N = 12, NYHA I (triangles), N = 19, NYHA II (crosses) and N = 19, NYHA III (circles). Estimated regression equation for VO_2peak: 8.9 + 0.098 x walking time; (R = 0.73; $P < 0.001$).

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ORIGINAL ARTICLE

The 6-min walk test in heart failure: is it a max or sub-maximum exercise test?

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Abstract The aim of the study is to compare the cardiorespiratory response during the 6-min walk test (6MWT) with a symptom-limited cardiopulmonary exercise test (CPET) in patients with varying degrees of heart failure. Thirty-seven patients with heart failure (New York Heart Association I–III) were asked to complete a 6MWT and a CPET on a cycle ergometer. Respiratory gases were measured during both the tests and patients were grouped into tertiles according to their VO_{2peak} reached during the CPET prior to performing statistical analysis of all other respiratory parameters. Patients were grouped into the following tertiles: Group 1 (VO_{2peak} >25.2 ml/kg per min, $N = 13$), Group 2 (VO_{2peak} >17.5–25.2 ml/kg per min), and Group 3 (VO_{2peak} ≤17.5 ml/kg per min). Despite the good overall correlation between 6MWT VO_2 and CPET VO_{2peak} ($r = 0.72$, $P < 0.001$), significant differences were seen within Groups 1 and 3 ($P < 0.05$). In Group 1, 6MWT VO_2 was significantly lower compared with CPET VO_{2peak}, whereas Group 3 showed significantly higher 6MWT VO_2 compared with CPET VO_{2peak}. In conclusion, the use of the 6MWT to evaluate exercise capacity in patients with heart failure is highly dependent on the degree of functional impairment. In patients with advanced heart failure, the 6MWT elicits a maximum exercise response, whereas it only constitutes a sub-maximal exercise test in patients with mild heart failure and no functional limitations. This must be taken into consideration when using the 6MWT in large epidemiological studies to evaluate therapy outcome and clinical prognosis in patients with varying degrees of clinical disabilities.

Keywords Clinical exercise testing · Ventilatory response · Oxygen consumption · Exercise capacity

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Introduction

Maximal exercise capacity is an important prognostic parameter in chronic heart failure (CHF) used clinically to predict therapy outcome and survival rate in these patients (Bittner 2003; Cahalin et al. 1996). The gold standard for measuring exercise capacity (VO_{2peak}) is by cardiopulmonary exercise testing (CPET) performed either on a treadmill or on a cycle ergometer (Rostagno et al. 2003). In the US, treadmill protocols, such as a modified Bruce test, are the preferred exercise tool to determine the exercise capacity in patients with heart failure, whereas in several European countries bicycle exercise testing (ramp protocol 10 W/min) is predominantly used (Working Group on Cardiac Rehabilitation and Exercise Physiology and Working

Group on Heart Failure of the European Society of Cardiology 2001). Although prognostic information obtained from both testing modes is similar, it has been shown that patients achieve a higher VO_{2peak} on the treadmill ('true' VO_{2peak}) than on the bicycle (Maeder et al. 2008).

Owing to time and costs involved, CPET is not always feasible in large epidemiological studies in which significant numbers of patients are evaluated. In this case, CPET is frequently supported or substituted with the 6-min walk test (6MWT) in order to document changes in exercise capacity post intervention and during sequential follow ups. Test outcome in terms of total distance walked (m) is taken as an indicator of functional exercise capacity and clinically useful in terms of short-term prognosis and mortality (Rostagno et al. 2003). Moreover, many believe that tests, in which subjects with cardiac dysfunction can choose their own workload, are a better reflection of the individual's symptomatic impairment than a CPET (Guyatt et al. 1985; Lipkin et al. 1986; Riley et al. 1992). Steady-state exercise dynamics are more easily attained during a constant work load exercise test than during a CPET with steadily increasing work loads (Faggiano et al. 1997; Gayda et al. 2004). Although normally considered a sub-maximal exercise test in most healthy individuals, the 6MWT can pose as an intense physical challenge in patients with functional limitations such as those seen in heart failure (Lipkin et al. 1986; Zugck et al. 2000).

The purpose of this study was to compare the cardiorespiratory response during the 6MWT and a CPET assessed by cycle ergometry in patients with different stages of CHF. We wanted to investigate whether patients approach maximum respiratory parameters during the 6MWT similar to those measured by cycle ergometry and/or, if possible, might even reach higher peak respiratory parameters during the 6MWT. This has important clinical implications when deciding to use the 6MWT in large epidemiological studies to document clinical progress and evaluate therapy outcome in patients with varying degrees of heart failure.

Methods

Patient recruitment

Forty subjects were initially recruited with the cooperation of a heart failure outpatient clinic at the local university hospital. However, three patients were retrospectively excluded do to insufficient exercise time (<6 min) during the CPET and by not having met exhaustion criteria as listed below. The study complies with the Declaration of Helsinki and was approved by the local university's ethics committee. Inclusion criteria were mild to moderate stable heart failure defined by New York Heart Association (NYHA) class I–III, regardless of age and medical history, and willingness to participate in further clinical and laboratory analyses. Exclusion criteria were any unstable medical conditions that were contraindicative to exercise testing or if patients were unable to walk without assistance. Patients had previously been examined at the outpatient clinic and were scheduled for their quarterly follow-up. NYHA class had been pre-assigned by the clinic's attending physician based on the medical history and clinical follow ups. Once included, patients signed an informed consent and were re-examined by two independent physicians blinded to the results of the initial NYHA classification. This included medical history, self-perceived exercise tolerance, echocardiography, and laboratory parameters. Exercise tests were administered in a random order with at least 2 h of rest between CPET (VO_{2peak}) and the 6-min walk test (6MWT VO_2). All patients were familiar with exercise testing procedures and had previously performed both the tests.

Exercise testing

Cycle ergometry

Each subject undertook a symptom-limited CPET (ramp protocol 10 W min^{-1}) using an electronically operated cycle ergometer (Sport Excalibur, Lode Medical technology, Groningen, the Netherlands). This protocol was chosen based on the European recommendations for exercise testing in heart failure patients (Working Group on Cardiac Rehabilitation and Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology 2001). The test was performed in the early afternoon under non-fasting conditions and subjects were encouraged to exercise to exhaustion or until signs of severe arrhythmias or ischemia developed. Gases were analyzed via ZAN metabolic cart (ZAN 600 USB CPX, nSpire Health GmbH, Germany). VO_2 and VCO_2 were measured every 10 s and peak oxygen uptake (VO_{2peak}) was defined as the highest oxygen uptake reached during the CPET. Heart rate was measured on a 12-lead ECG and the electrocardiogram was monitored continuously. Perceived exertion using the Borg scale (6–20) was recorded at the end of each stage. Blood pressure was measured at rest, in 1-min intervals at the end of each exercise stage and in 2-min intervals during the recovery phase. The anaerobic threshold (AT) was defined using computer software (ZAN WINGPI 3.00) and maximal exertion was defined as meeting the following exhaustion criteria: (1) respiratory exchange ratio, RER >1.0, (2) Borg ≥18, (3) pedaling frequency ≤60 rpm.

Minute walk test

In preparation of the 6MWT, patients were required to wear a tightly fitted face mask and a 2.5-kg heavy back pack that

contained a portable ergospirometer (ZAN600 Mobile, nSpire Health GmbH, Oberthulba, Germany) to measure the metabolic gas exchange. The device has been validated and was calibrated against a known concentration and volume before each 6MWT. VO_2 and VCO_2 were measured every 10 s and peak oxygen uptake (6MWT VO_2) was defined as the highest oxygen uptake reached during the 6MWT. Measurements were continuously transmitted via radio antenna and retrospectively viewed and analyzed with customized computer software (ZAN WINGPI 3.00). Three minutes of pre-exercise respiratory gases (1 min of sitting and 2 min of standing) were collected prior to commencing the 6MWT test, followed by 4 min of post exercise respiratory gases during which patients were seated.

The 6MWT was conducted in an enclosed corridor on a pre-measured test course that was 40 m in length. The course was marked every 5 m and subjects were instructed to walk from one end to the other end, covering as much distance as possible during the 6 min, but reminded to pace themselves in order to complete the full 6 min. Subjects were allowed to rest if needed and remaining time was called out every minute. Upon test completion, total walking distance (m) was recorded.

Data analysis

Statistical analysis was carried out using SPSS software (version 15.0, SPSS Inc.). Data were descriptively analyzed reporting mean ± standard deviation (SD) for quantitative measurements and percentages for frequencies. Bivariate correlations of continuous variables were investigated using Pearson's correlation coefficient (r). Statistical comparisons between two related measurements were assessed by paired Student's t test. The χ^2 test was used to compare frequencies between independent samples. Patients were grouped into tertiles according to their VO_{2peak} reached during the CPET. All statistical analyses were based on this classification system. To account for multiple comparisons, differences between peak VO_2 groups were assessed using analysis of variance followed by unpaired Student's t test in terms of a hierarchical test procedure. In all data analyses, P values <0.05 were considered as statistically significant and were reported in an explorative manner. The trend of parameter development was displayed by line graphs of means with 95% confidence intervals.

Results

Classification by tertiles yielded: Group 1 ($N = 13$): VO_{2peak} >25.2 ml/kg per min; Group 2 ($N = 12$): VO_{2peak} >17.5–25.2 ml/kg per min; Group 3 ($N = 12$): VO_{2peak} ≤17.5 ml/kg per min. According to this categorization principle, all patient base line characteristics are listed in Table 1. Sixty-two percent (8/13 patients) in Group 1 were diagnosed with heart failure due to causes of ischemic heart disease with a preserved EF (≥45%) and normal VO_{2peak} (diastolic heart failure), whereas Groups 2 and 3 consisted mostly of patients with ischemic and/or dilated cardiomyopathy secondary to ventricular systolic dysfunction (EF ≤45%). Table 2 lists maximal respiratory parameters attained during the 6 MWT compared with maximum (peak) and AT values reached during the CPET. Mean CPET duration was 13.6 ± 2.6 min in Group 1 patients (range 11.0–19.0 min, median 12.5 min), 12.9 ± 2.5 in Group 2 patients (range 9.0–17.5 min, median 13.0), and 8.9 ± 2.4 min in Group 3 patients (range 6.0–12.5 min, median 8.5 min).

A strong overall correlation between 6MWT VO_2 and CPET VO_{2peak} was seen for all study participants ($r = 0.72$, $P < 0.001$) (Fig. 1), which was supported by a similarly strong correlation between CPET VO_{2peak} and 6MWT distance ($r = 0.77$, $P < 0.001$) and 6MWT VO_2 and 6MWT distance ($r = 0.82$, $P < 0.001$). Nevertheless, marked intra-group differences for peak oxygen uptake reached during the 6MWT compared with the CPET were observed (Fig. 2), reaching statistical significance in Groups 1 and 3 ($P < 0.05$), but not in Group 2 ($P = 0.2$). This indicates that the 6MWT does not elicit the same exercise response in all heart failure patients, but it is dependent on the degree of functional limitation.

6MWT oxygen uptake (6MWT VO_2) was similar to CPET VO_{2AT} for Group 1 with a mean difference of −1.4 ± 4.4 ml/kg per min ($P = 0.1$), but significantly below CPET VO_{2peak} with a mean difference of −4.3 ± 3.1 ml/kg per min ($P < 0.001$). In Group 2, 6MWT VO_2 was significantly above CPET VO_{2AT} with mean difference: −3.5 ± 4.9 ml/kg per min ($P = 0.03$), but only slightly below CPET VO_{2peak} with mean difference: −2.9 ± 7.3 ml/kg per min ($P = 0.2$). Finally in Group 3, 6MWT VO_2 was significantly above CPET VO_{2AT} and CPET VO_{2peak} with mean differences: −3.7 ± 3.0 ml/kg per min ($P = 0.001$) and 1.8 ± 2.9 ml/kg per min ($P = 0.049$), respectively. These data suggest that the 6MWT does not elicit a maximum exercise response in patients with mild heart failure and no functional limitations, approaches a near maximum exercise test in patients with moderate heart failure, and reaches a maximum exercise test in patients with advanced heart failure with 6MWT VO_2 significantly above CPET VO_{2peak}.

The degree of physical exertion is further underlined by the VO_2/VCO_2 ratio, also referred to as the RER. In Group 1, 6MWT RER was well below both CPET RER_{AT} and CPET RER_{peak} with mean differences of 0.11 ± 0.06 ($P < 0.001$) and 0.23 ± 0.06 ($P < 0.001$), respectively. In Group 2, 6MWT RER was similar to CPET RER_{AT} with a mean difference of 0.04 ± 0.09 ($P < 0.13$), but significantly

Table 1 Patients characteristics

	Group 1 $N = 13$	Group 2 $N = 12$	Group 3 $N = 12$	Total $N = 37$	P value
Gender					
Men	11 (85%)	9 (77%)	9 (71%)	29 (78%)	0.71
Women	2 (15%)	3 (23%)	3 (29%)	7 (22%)	
Age (years)	64.1 ± 14.9	59.0 ± 13.6	59.8 ± 12.5	61.1 ± 13.5	0.62
BMI (kg/m^2)	26.0 ± 2.3	28.6 ± 5.2	30.9 ± 3.5[b]	28.4 ± 4.2	0.01
Maximal work load (W)	136 ± 25.7	129 ± 25.3[a]	89.2 ± 24.3[b]	119 ± 32.1	<0.01
Mean CPET exercise time (min)	13.6 ± 2.6	12.9 ± 2.5[a]	8.9 ± 2.4[b]	11.9 ± 3.1	<0.01
6 MWT distance (m)	619 ± 90.8	560 ± 63.3[a]	381 ± 102[b]	523 ± 133	<0.01
LVEF (%)	46.4 ± 13.3	38.0 ± 14.1	34.4 ± 10.3[b]	39.8 ± 13.4	0.07
LVEDD (mm)	58.9 ± 10.1	63.4 ± 13.9[a]	74.4 ± 11.4[b]	65.4 ± 13.3	<0.01
NT-proBNP (pg/ml)	834 ± 1,034	1,328 ± 1,153	1,927 ± 1,594[b]	1,349 ± 1,321	0.12
Medication					
ACE inhibitor	9 (69%)	12 (100%)	11 (92%)	32 (87%)	0.045
Beta blocker	11 (75%)	11 (89%)	10 (83%)	32 (87%)	0.73
Digitalis	2 (15%)	0	4 (33%)	6 (16%)	0.12
Diuretics	7 (54%)	11 (92%)	12 (100%)	30 (81%)	<0.01
Diagnosis					
HFPEF	8 (62%)	1 (8%)	0	9 (26%)	<0.01
ICM	4 (31%)	4 (33%)	2 (17%)	10 (27%)	<0.01
DCM	1 (8%)	7 (58%)	10 (83%)	18 (49%)	0.03

Clinical characteristics of study population

Data are presented as mean ± standard deviation

Overall group comparison by ANOVA/χ^2 test

LVEF left ventricular ejection fraction (%), *LVEDD* left ventricular end diastolic diameter, *ACE inhibitor* angiotensin converting enzyme inhibitor, *HFPEF* heart failure with preserved EF, *ICM* ischemic cardiomyopathy, *DCM* dilated cardiomyopathy

Post hoc group differences with $P < 0.05$: [a]Group 2 versus Group 3; [b]Group 3 versus Group 1

below CPET RER_{peak} with a mean difference of 0.15 ± 0.1 ($P < 0.001$). Finally, in Group 3, 6MWT RER was well above CPET RER_{AT} with a mean difference of −0.08 ± 0.12 ($P = 0.05$), and almost identical to CPET RER_{peak} with a mean differences of 0.01 ± 0.14 ($P = 0.78$).

The VE/VCO_2 ratio during the 6MWT, indicating ventilatory efficiency, was similar to CPET VE/VCO_{2AT} in Groups 1 and 2 with mean differences of −0.2 ± 4.9 ($P = 0.9$) and −0.65 ± 2.9 ($P = 0.5$), respectively. 6MWT VE/VCO_2 was significantly below CPET VE/VCO_{2peak} for Group 1 (mean difference −4.3 ± 5.4, $P = 0.014$), but not Group 2 (mean difference −1.4 ± 3.4, $P = 0.19$). In Group 3, 6MWT VE/VCO_2 was below both CPET VE/VCO_{2AT} and CPET VE/VCO_{2peak} with mean differences of −2.2 ± 6.4 ($P = 0.3$) and −4.9 ± 9.3 ($P = 0.09$), respectively.

Detailed VO_2 uptake during the 6MWT was mediated at 30 s and is plotted in Fig. 3 (mean ± 2SD). Patients with markedly reduced exercise capacity (Group 3) showed an attenuated increase in VO_2 uptake at the beginning of exercise and a flatter decline of VO_2 after exercise cessation back towards baseline values compared with Groups 1 and 2 patients.

Discussion

The results of this present study suggest that patients with heart failure and markedly reduced exercise capacity (VO_{2peak} ≤17.5 ml/kg per min) are able to reach significantly higher peak respiratory parameters during the 6MWT than during CPET on a cycle ergometry. The opposite was true for patients with only mild heart failure and no functional limitations (VO_{2peak} >25.2 ml/kg per min). Here, clearly longer exercise durations at higher work rates were required to elicit a peak exercise response as defined by CPET VO_{2peak} and 6MWT respiratory parameters were significantly below those attained during cycle ergometry. Patients with mild to moderate heart failure (VO_{2peak} >17.5–25.2 ml/kg per min) showed a similar exercise response during both the 6MWT and cycle ergometry.

Table 2 Respiratory kinetics

	Group 1 $N = 13$	Group 2 $N = 12$	Group 3 $N = 12$	Total $N = 37$	P value
VO_2 (ml/kg per min)					
6MWT	23.4 ± 2.6[a]	20.4 ± 2.5[b]	15.5 ± 3.6[c]	19.8 ± 4.4	<0.01
CPET AT	22.9 ± 5.05[a]	16.9 ± 4.1[b]	11.8 ± 2.1[c]	17.0 ± 5.7	<0.01
CPET peak	27.6 ± 3.3[a]	23.3 ± 7.2[b]	13.6 ± 2.5[c]	21.7 ± 7.6	<0.01
VCO_2 (ml/kg per min)					
6MWT	20.5 ± 2.8	18.7 ± 2.4[b]	15.7 ± 3.1[c]	18.4 ± 3.6	0.01
CPET AT	21.2 ± 5.4[a]	16.4 ± 4.3[b]	11.2 ± 2.3[c]	16.4 ± 5.9	<0.01
CPET peak	30.9 ± 6.13[a]	24.8 ± 7.2[b]	14.2 ± 2.9[c]	23.5 ± 9.0	<0.01
RER					
6MWT	0.87 ± 0.05	0.92 ± 0.05[b]	1.03 ± 0.09[c]	0.94 ± 0.09	<0.01
CPET AT	0.98 ± 0.05	0.96 ± 0.08	0.95 ± 0.05	0.97 ± 0.06	0.35
CPET peak	1.10 ± 0.08	1.07 ± 0.07	1.03 ± 0.04[c]	1.07 ± 0.07	0.05
VE (L/min)					
6MWT	43.3 ± 7.3	44.4 ± 12.4	42.9 ± 7.6	43.5 ± 9.1	0.91
CPET AT	44.2 ± 11.2	38.4 ± 9.1	34.8 ± 14.3	39.3 ± 12.0	0.15
CPET peak	75.7 ± 18.7[a]	59.2 ± 13.4	46.2 ± 16.5[c]	60.8 ± 20.2	<0.01
VE/VCO_2					
6MWT	27.3 ± 3.3	28.0 ± 3.2	31.5 ± 5.7[c]	28.6 ± 4.5	0.04
CPET AT	27.4 ± 4.8	28.6 ± 3.3[b]	33.7 ± 4.6[c]	29.9 ± 5.0	<0.01
CPET peak	31.6 ± 5.3	29.4 ± 4.1[b]	36.2 ± 9.7	32.3 ± 7.2	0.04
VE/VO_2					
6MWT	23.8 ± 3.1	25.8 ± 3.2[b]	32.5 ± 7.8[c]	27.3 ± 6.3	<0.01
CPET AT	26.1 ± 3.07	27.8 ± 4.4[b]	32.03 ± 5.3[c]	28.6 ± 4.8	<0.01
CPET peak	34.1 ± 4.3	31.5 ± 5.1[b]	38.2 ± 9.7	34.6 ± 8.1	0.12

Maximal respiratory parameters during the 6MWT and the CPET assessed by ergometry

AT anaerobic threshold, *peak* maximal values, VO_2 oxygen consumption, VCO_2 carbon dioxide production, *RER* respiratory exchange ratio, *VE* ventiliation, VE/VCO_2 ventilatory efficiency, VE/VO_2 ventilatory equivalent

Overall group comparison by ANOVA

Post hoc group differences with $P < 0.05$: [a]Group 1 versus Group 2; [b]Group 2 versus Group 3; [c]Group 3 versus Group 1

Therefore, the use of the 6MWT to evaluate VO_{2peak} seems highly dependable on the degree of functional limitation in patients with heart failure. It seems suitable in patients with moderate to more advanced stages of heart failure, however, not in patients with mild heart failure and no functional limitations.

Previous studies were able to show that the majority of patients with heart failure achieve higher VO_{2peak} on the treadmill than on the cycle ergometer (Maeder et al. 2008). Our data suggest similar might be true for the 6MWT in those patients with 6MWT distances at or below 400 m. Faggiano et al. (1997) analyzed 26 patients with CHF and found 73% to be above AT during the 6MWT and 27% to have a higher end 6MWT VO_2 than VO_{2peak}. Similarly, Foray et al. (1996) reported the 6MWT ventilatory demand to be ≥85% of VO_{2peak} in heart failure patients with implantable cardiac assist devices; thus, questioning the suitability of the 6MWT as a sub-maximal exercise test. Kervio et al. (2004) compared healthy subjects to heart failure patients grouped according to receiving cardiac resynchronization therapy (CRT) and found 6MWT intensity to be above the ventilatory threshold and around 90% of VO_{2peak} for CRT-treated patients compared with 70% of VO_{2peak} in age-matched individuals.

With the presumption that patients performed both exercise tests at maximal effort, one would expect 6MWT VO_2 to approach CPET VO_{2peak} in patients with limited exercise capacity. This is due to the nature of the test protocol where the level of effort is set by the patient as opposed to the protocol (i.e. constant load exercise test vs. ramp protocol). The significantly higher peak 6MWT VO_2 compared with CPET VO_{2peak} in patients with advanced heart failure suggests that a constant load exercise test might enable improved ventilatory efficiency in these patients. This is not true for patients with mild heart failure and no functional limitations, in which longer exercise durations at higher work loads are needed to elicit a maximum exercise response.

Many patients with heart failure suffer from severe muscular atrophy making it difficult for them to produce the necessary leg power required during a CPET to work against the increase in resistance (Pu et al. 2001). The fixed ramp protocol used in this study might have prevented individuals with advanced heart failure from reaching maximum exercise due to premature muscular leg fatigue. Previous investigators have demonstrated VO_{2peak} to be dependable on total exercise duration in patients with heart failure (Agostoni et al. 2005) and the recommended time to

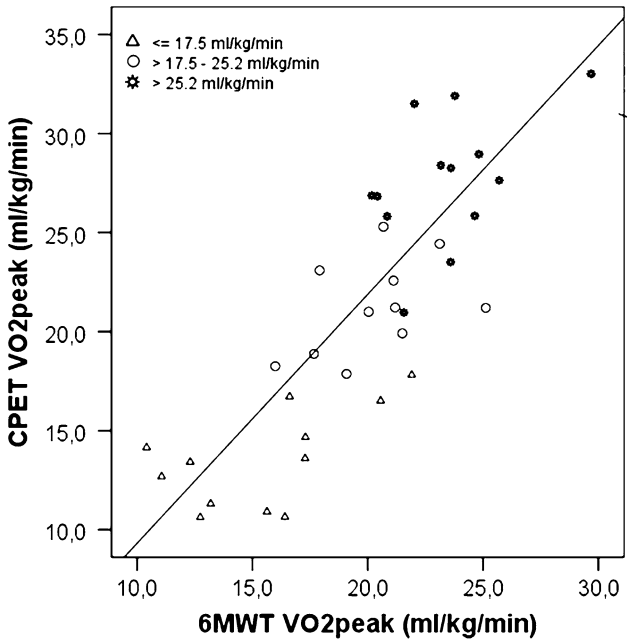

Fig. 1 Correlation of 6MWT VO_2 and CPET VO_{2peak}. Correlation of 6MWT VO_2 and CPET VO_{2peak} assessed during ergometry ($r = 0.72$; $P < 0.001$). Values are displayed in ml/kg per min. ☼ Group 1 ($n = 13$): VO_{2peak} >25.2 ml/kg per min; *open circle* Group 2 ($n = 12$): VO_{2peak} >17.5–25.2 ml/kg per min; *delta* Group 3 ($n = 12$): VO_{2peak} ≤17.5 ml/kg per min

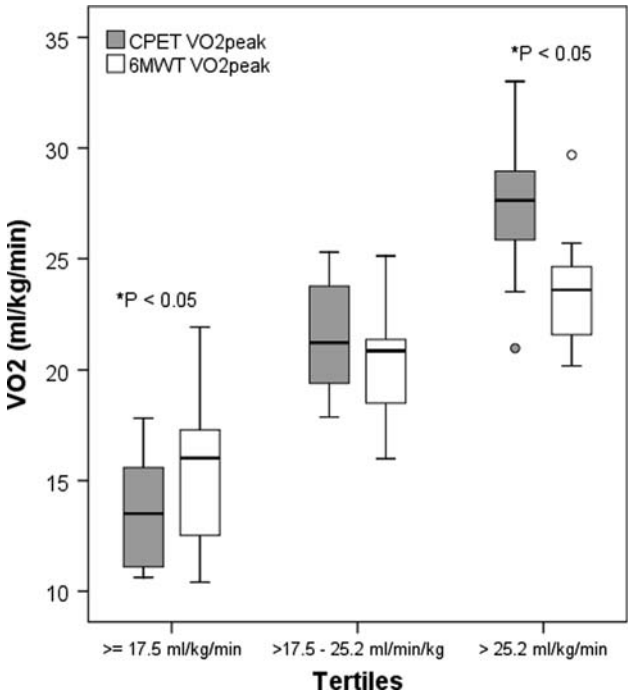

Fig. 2 Boxplot of 6MWT VO_2 and CPET VO_{2peak}. Comparison of mean values for CPET VO_{2peak} (*gray boxes*) and 6MWT VO_2 (*white boxes*) for each group. Values are displayed in ml/kg per min. Differences in CPET VO_{2peak} and 6MWT VO_2 reached statistical significance for Groups 1 and 3 ($P < 0.05$)

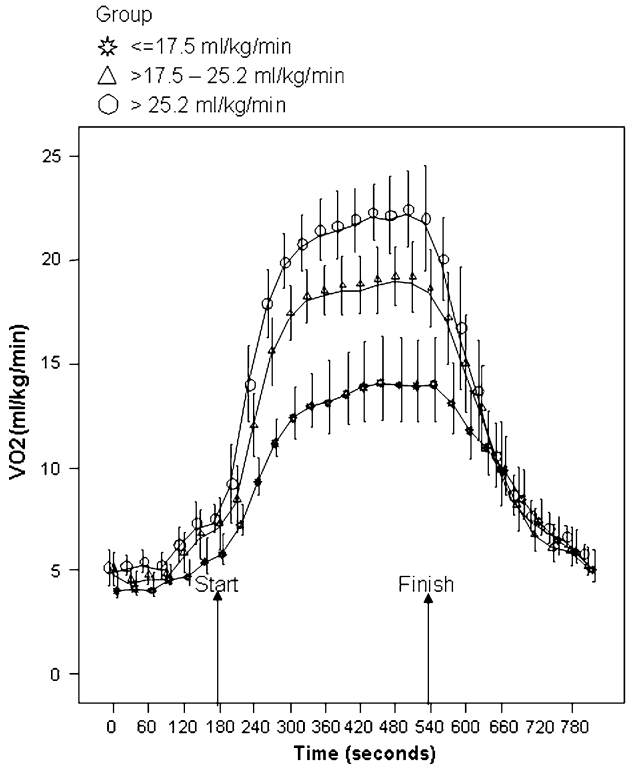

Fig. 3 Oxygen uptake during the 6MWT. Detailed analysis of oxygen uptake during the 6MWT (6MWT VO_2) averaged over 30-s intervals. Group means are plotted with 95% confidence intervals (mean ± 2SE). *Open circle* Group 1 ($n = 13$): VO_{2peak} >25.2 ml/kg per min; *delta* Group 2 ($n = 12$): VO_{2peak} >17.5–25.2 ml/kg per min; ☼ Group 3 ($n = 12$): VO_{2peak} ≤17.5 ml/kg per min

elicit VO_{2peak} in these patients is said to be between 10 and 15 min (Working Group on Cardiac Rehabilitation and Exercise Physiology and Working Group on Heart Failure of the European Society of Cardiology 2001). In this study, mean cycle duration approximated 9 min in patients with more advanced heart failure. Therefore, it is possible that total cycle time in these patients was insufficient to overcome the attenuation in oxygen delivery typically associated with a more severe clinical status, thereby preventing VO_{2peak} to be attained (Casaburi et al. 1989; Cleuziou et al. 2005). An individualized ramp protocol taking into account the degree of functional limitations and clinical disabilities of our study population might have been more appropriate and might have minimized this problem (Clark and Coats 2000).

The heterogeneity in our study population regarding heart failure etiology is a further limitation of this study. 8/13 Group 1 patients had heart failure due to ischemic heart disease with a preserved EF (HFPEF) or diastolic heart failure. This explains the near normal VO_{2peak} values in these patients. Although clinical features in patients with heart failure are similar, patients with HFPEF tend to have better functional capacity compared with patients with heart failure

secondary to systolic dysfunction (Rostagno et al. 2003). Thus, it is possible that differences in etiology account for some of the differences found among study participants.

We not only compared two different exercise modes (cycling vs. walking), but also two different exercise protocols (constant load 6MWT vs. maximum incremental cycle test) in this study. Therefore, our results should be interpreted with caution. The use of an individualized ramp protocol on a treadmill would have been more suitable in order to compare the cardiorespiratory response between CPET and the 6MWT. Finally, exercise tests should have been administered on separate days to avoid a carry over of fatigue from one test to another. Although offered none of the participants felt this to be necessary. We did perform a separate analysis of peak respiratory parameters including only those patients on beta blockers ($n = 32$, 86%) to account for any possible influences of medication on test results. However, this did not significantly change any of the presented findings.

In conclusion, judging across the spectrum of heart failure defined by VO_{2peak}, the use of the 6MWT to assess peak exercise capacity seems highly dependable on the degree of functional limitation. In this study, patients with advanced heart failure reached higher 6MWT VO_2 compared with CPET VO_{2peak} assessed by cycle ergometry. In contrast, it only served as a sub-maximal exercise test in patients with mild heart failure and no functional limitations. This should be taken into consideration when using the 6MWT in large epidemiological studies to evaluate therapy outcome post intervention and/or monitor clinical prognosis in patients with varying degrees of heart failure. However, these findings are preliminary and must be evaluated in a larger patient population.

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Conflict of interest statement None declared.

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