Activity behaviours and quality of life in patients with malignant pleural effusion

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Patients with malignant pleural effusion in Hong Kong demonstrate high sedentary behaviours and minimal physical activity which correlate to important dimensions of quality of life. Clinician-rated performance status was not reflected in accelerometer data. https://bit.ly/3zLD2Hl

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Abstract

Background and objective Accelerometery is used to measure activity behaviours in patients with malignant pleural effusion (MPE). This study aimed to evaluate physical activity and sedentary behaviour profiles of patients with MPE in Hong Kong, and to explore relationships between activity behaviours and quality of life (QoL). We also compared clinician-recorded performance status measures with objective measures of activity levels.

Methods Participants wore an Actigraph GT3X+ accelerometer continuously for 7 consecutive days. The EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L) was used to assess five dimensions of QoL and correlate with activity behaviours. The Eastern Cooperative Oncology Group (ECOG) performance status was documented by clinicians at baseline.

Results Fifty-one patients with MPE received accelerometers; 94% had ⩾1 valid day of data. Participants spent 76% (SD 2.32) of waking hours sedentary, 23% (SD 1.40) of waking hours in light activity and 0.3% (median, interquartile range 0.0–1.5) in moderate-to-vigorous physical activity (MVPA). Higher light activity and MVPA behaviours were associated with increased participation in self-care tasks (r_s=−0.43, p=0.003; r_s=−0.45, p=0.001, respectively) and usual activities (r_s=−0.42, p=0.003; r_s=−0.45, p=0.001, respectively). Patients with an ECOG status of 0 or 1 spent an average of 75% of waking hours sedentary.

Conclusion This is the first report of physical activity behaviours in patients with MPE in Hong Kong, demonstrating high sedentary behaviours and low physical activity which correlated to dimensions of QoL. Clinician-rated performance status was not reflected in accelerometery data, suggesting a discrepancy between performance status measures and objective measures of activity in patients with MPE.

Introduction

Malignant pleural effusion (MPE) is a clinical complication attributed to primary pleural cancer (*e.g.* mesothelioma) or the metastatic advancement of cancer, most commonly lung, breast and gynaecological cancers [1, 2]. The presence of MPE indicates incurable disease, with limited treatment options. Median patient survival is generally 9–12 months from first presentation [1]. This patient group commonly report pain and debilitating breathlessness which can contribute to reduced quality of life (QoL) [3].

Performance status measures are widely used in cancer populations [4–6] including patients with MPE [7], to assess eligibility for clinical trials and as a predictor of survival. These performance status scales typically range from 0–4, and clinicians estimate a patient's ability to perform activities of daily living. However, the subjective interpretation of these measures can vary between raters resulting in inconsistencies [8]. Further, such scales may not identify small but potentially meaningful changes in function. Due to the clinical use of performance status measures to determine eligibility for clinical procedures and trials, performance status measurements need to be improved from gross and subjective measures to better represent true performance status.

The use of accelerometers continues to grow as they provide a more reliable objective measure of daily activity behaviours in MPE populations [7]. Accelerometers are small wearable devices that measure movement related to physical activity and capture sedentary behaviours. Activity behaviours can be categorised as a physical activity behaviour (including low intensity physical activity and moderate-to-vigorous physical activity (MVPA)) and sedentary behaviour (*i.e.* low energy expenditure tasks including sitting or reclining activities) during waking hours [7]. A preliminary study of patients with MPE living in Australia demonstrated that this cohort have low activity levels, spending most of their waking hours sedentary [7].

The aims of this study were to evaluate physical activity and sedentary behaviour profiles of patients with MPE living in Hong Kong, and to explore relationships between activity behaviours and QoL. We also aimed to compare performance status measures with objective measures of activity levels.

Methods

Setting and participants

This cross-sectional study recruited patients with MPE from three hospitals in Hong Kong. Patients with a diagnosis of an MPE were eligible for entry. MPE was defined as the presence of malignant cells in the pleural fluid or pleural tissues, or the presence of a large exudative pleural effusion without other causes in a patient with known disseminated extra-thoracic malignancy [7]. Exclusion criteria were age younger than 18 years, pleural inflection, pregnant or lactating women, inability to consent or comply with the protocol, and anticipated pleural drainage procedure within 1 week of recruitment. The study was approved by the Institutional Review Board of the University of Hong Kong (#UW 17-516).

Procedures

Eligible participants who agreed to participate and provided written informed consent were provided with accelerometers at outpatient appointments and were asked to wear the accelerometers around the waist for 24 h per day for 7 consecutive days. Demographic and medical data were obtained from medical records.

Outcomes

Activity behaviours were measured by triaxial accelerometer assessment (ActiGraph GT3X+ Pensacola, FL, USA). The accelerometers were programmed to record raw data at a frequency of 30 Hz and vertical axis movement counts per 60-second epoch. An established algorithm [9] was used to process the accelerometer data in SAS (version 9.3, SAS Institute, Cary, NC, USA). A valid day of data was defined as 8 h of waking wear time [10]. Accelerometer data with a minimum of 1 day of valid data were included. Results were presented as percentage of waking wear time, calculated as the time variable divided by wear time. Sedentary-to-light ratio was calculated as the percentage of waking hours spent sedentary divided by the percentage of waking hours spent in light activity. Higher numbers signified more waking hours spent sedentary relative to light activity.

The EuroQoL 5 Dimensions 5 Levels (EQ-5D-5L) was used to assess five dimensions of QoL (*i.e.* mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Items were graded from "no problems" to "unable to/extreme problems", with lower scores indicating better QoL [11, 12]. The EQ-5D-5L index score was calculated based on Hong Kong specific value sets, with higher index scores reflecting a better health state [13].

The Eastern Cooperative Oncology Group (ECOG) performance status scale [14] was used by clinicians to conjecture patient participation in daily activities. Grade 0 referred to patients who were "fully active, able to carry on all pre-disease performance without restriction"; Grade 1 to those "restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, *e.g.* light house work, office work"; Grade 2 as "ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours"; Grade 3 as "capable of only limited self-care; confined to bed or chair more than 50% of waking hours"; and Grade 4 as "completely disabled; cannot

carry out any self-care; totally confined to bed or chair" [14]. Good performance status was defined as an ECOG performance status of 0–1; and an ECOG score of ⩾2 was defined as a poor performance status.

Statistical analysis

Statistical analyses were conducted using the Statistical Package for the Social Sciences (v. 28, IBM Corporation, Somers, NY, USA). Data were tested for normality and reported using mean (SD) or median (interquartile range (IQR)) as appropriate. Pearson correlation coefficient and Spearman rank order correlations were used to assess correlation between activity behaviours and QoL. Between-group comparisons of performance status were performed by the Mann–Whitney U-Test. An alpha of 0.05 was used to determine statistical significance.

Results

Participant flow through the accelerometery assessment is demonstrated in figure 1. The majority of participants were compliant with the assessment; 94% had ⩾1 day of valid data, and 88% had ⩾4 days of valid data. The median days of valid assessment was 6 (IQR 5–7), and the average waking wear time was 13.7 (SD 2.0) hours per day.

Baseline characteristics of the participants are reported in table 1. The participants were predominantly male (58%) and the median age was 66 years (IQR 57–75). The most common primary cancer was lung malignancy (79%) and 85% of participants had an ECOG performance status of 0 or 1. The most common active treatment received during the study period was chemotherapy (40%).

Cross-sectional analysis of physical activity and sedentary behaviour

Activity behaviour outcomes are presented in table 2. Participants spent an average of 76% of time sedentary (SD 2), 23% of time in light physical activity (SD 1) and a median of 0.3% of time engaging in MVPA (IQR 0.0–1.5), as a proportion of waking hours. The median step count was 5852 steps/day (IQR 2349–9149).

Association between QoL and activity behaviours

Correlations between dimensions of QoL and activity behaviours are reported in table 3. Increased time spent in light activity and MVPA were associated with better ability to perform self-care tasks (r_s=−0.43, p=0.003; r_s=−0.45, p=0.001, respectively). Conversely, increased sedentary behaviour was associated with lower ability to undertake self-care tasks (r_s=0.41, p=0.004).

Higher proportions of time spent in light activity and MVPA were significantly associated with better involvement in usual activities (r_s=−0.42, p=0.003; r_s=−0.45, p=0.001, respectively). There were significant correlations between better participation in usual activities and increased time in bouts of light

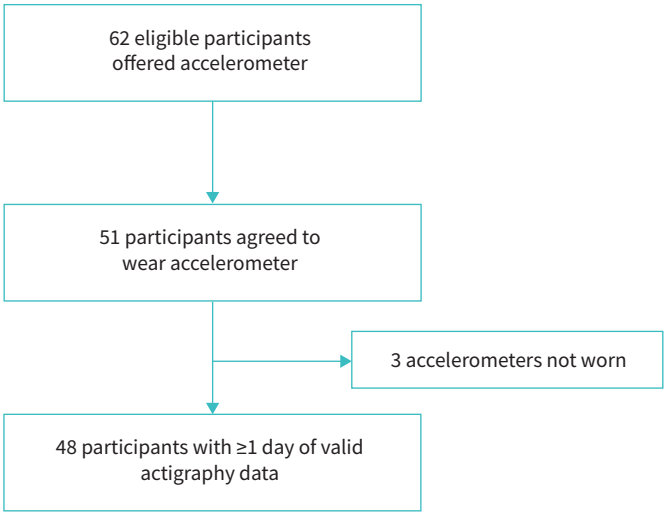

FIGURE 1 Participation flow chart.

TABLE 1 Baseline characteristics of 48 participants

Characteristic	Total
Age (years)[#]	66 (57–75)
Men	28 (58%)
Primary diagnosis	
Lung cancer	38 (79%)
Mesothelioma	4 (8%)
Other malignancy	6 (13%)
Body mass index[#] (n=47)	21 (19–23)
ECOG baseline	
0–1	41 (85%)
⩾2	7 (15%)
Comorbidities	
Respiratory	6 (13%)
Cardiac	14 (29%)
Acute renal failure	1 (2%)
Hypoalbuminaemia	9 (19%)
Diabetes	6 (13%)
Depression	5 (10%)
Smoking status	
Current smoker	3 (6%)
Ex smoker	14 (29%)
Pack-years[#]	30 (6–45)
Effusion (n=47)	
Left sided	18 (38%)
Right sided	26 (54%)
Bilateral	3 (6%)
Loculations	7 (15%)
IPC *in situ* during study period	3 (6%)
Previous IPC	4 (8%)
Trapped lung	9 (19%)
Achieved pleurodesis	8 (17%)
Dyspnoea (VAS score, 0–100)[#,¶]	55 (24–76)
Active treatment during study period	
Chemotherapy	19 (40%)
Immunotherapy	1 (2%)

Data are presented as n (%), unless otherwise indicated. ECOG: Eastern Cooperative Oncology Group; IPC: indwelling pleural catheter; Previous IPC: IPC *in situ* within 12 months prior to study enrolment; VAS: visual analogue scale; [#]: data presented as median (interquartile range); [¶]: 0 signifying no dyspnoea.

activity <5 min (r_s=−0.40, p=0.005), 5–10 min of bouts of light activity (r_s=−0.53, p=0.001) and 10–20 min of bouts of light activity (r_s=−0.41, p=0.004). Increased time in 10–20 min of bouts of light activity also correlated to better ability to partake in self-care tasks (r_s=−0.50, p=0.001). Increased time in sedentary bouts over 60 min correlated with poorer participation in usual activities (r_s=0.44, p=0.002).

TABLE 2 Baseline actigraphy profile of 48 participants

Outcome	Assessment
Average waking wear time (hours)	13.7±2.0
Number of valid days[#]	6 (5–7)
Number of participants with ⩾4 valid days, n (%)	42 (88)
Sedentary time (% of waking hours)	76 (2)
Light activity time (% of waking hours)	23 (1)
MVPA time (% of waking hours)[#]	0.3 (0.0–1.5)
Sedentary-to-light ratio[#]	3.0 (2.4–4.9)
Step count[#]	5852 (2349–9149)

Data are presented as mean±SD unless otherwise indicated; MVPA: moderate-to-vigorous physical activity; [#]: data presented as median (interquartile range).

TABLE 3 Pearson correlation coefficient between activity behaviours and EQ-5D-5L dimensions

Activity behaviour outcome	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression	EQ-5D-5L index
Sedentary	0.17	0.41**	0.34*	0.02	−0.05	−0.31
Light activity	−0.25	−0.43**	−0.42**	−0.02	0.13	0.32
MVPA#	−0.27	−0.45**	−0.45**	−0.20	−0.04	0.37**
Sedentary-to-light ratio#	0.26	0.46**	0.42**	−0.01	−0.10	−0.22
Sedentary bout >60 min#	0.19	0.38**	0.44**	0.09	−0.01	−0.23
Light activity bouts <5 min	−0.17	−0.34*	−0.40*	−0.08	−0.02	0.36
Light activity bouts 5–10 min	−0.25	−0.39**	−0.53**	0.02	0.12	0.26
Light activity bouts 10–20 min#	−0.24	−0.50**	−0.41**	−0.02	0.12	0.22

EQ-5D-5L: EuroQoL 5 Dimensions 5 Levels; MVPA: moderate-to-vigorous physical activity; #: Spearman rank correlation; *: p<0.05; **: p<0.01.

Increased participation in MVPA was associated with a better overall health state on the EQ-5D-5L index (r_s=0.37, p=0.009). A less favourable sedentary-to-light ratio was associated with poorer participation in self-care and usual activity dimensions of QoL (r_s=0.46, p=0.001 and r_s=0.42, p=0.003, respectively).

Differences in activity behaviours, step count and QoL by performance status groups

Differences in activity behaviours based on ECOG are shown in table 4. Participants with a good ECOG performance status (0 or 1) had significantly higher median step count per day of 6331 (IQR 2703–9372), compared to 1238 (IQR 551–5835) steps by participants with a poor ECOG status of 2 or greater (p=0.022). There were no statistically significant differences between good and poor performance status groups for the proportion of times spent sedentary (75% *versus* 82%), light activity (24% *versus* 17%) or MVPA (0% *versus* 0%).

Discussion

This present study demonstrates accelerometery as a feasible method for evaluating physical activity and sedentary behaviours in patients with MPE living in Hong Kong. Our data demonstrates this cohort had low physical activity levels and spent most of their waking hours sedentary – standing still, sitting or lying down. Physical activity behaviours were correlated with QoL outcomes which raises the possibility that interventions which improve activity levels could result in improved QoL. Discrepancies exist between clinician documented ECOG performance status based on patient's reports and objective measures of physical activity levels.

Our data shows patients with MPE living in Hong Kong spent the majority of waking hours sedentary with limited participation in light activity. The results from this group were consistent with our prior studies of patients with MPE in Western Australia [7, 15, 16]. Throughout the 7-day accelerometer recording period, the mean MVPA time was only 10.8 min·day^{-1}. These results were comparable to a previously reported study of patients with MPE living in Australia, where the mean MVPA was 9.5 min·day^{-1} [7]. In our study, the majority of waking wear time comprised of sedentary behaviours, with patients spending an average of 76% or 10.4 h of their day sedentary. This result is comparable to patients with MPE living in Australia, who spent on average 72% of waking hours sedentary [7].

The low physical activity levels in patients with MPE may be explained by the high symptom burden associated with the disease. Debilitating breathlessness significantly impairs QoL in patients with MPE [17],

TABLE 4 Activity behaviour as a percentage of waking wear time, based on ECOG performance status

Activity	ECOG 0–1 (n=41)	ECOG ⩾2 (n=7)	p-value
Step count#	6331 (2703–9372)	1238 (551–5835)	p=0.020
Sedentary time	75±2	82±4	p=0.055
Light activity time	24±1	17±2	p=0.432
MVPA#	0 (0.00–0.22)	0 (0.00–0.05)	p=0.328
Sedentary-to-light ratio#	3.0 (2.31–4.81)	4.0 (2.83–23.76)	p=0.193

Data are presented as mean±SD unless otherwise stated. ECOG: Eastern Cooperative Oncology Group; MVPA: moderate-to-vigorous physical activity; #: data presented as median (interquartile range).

and is a predictor of survival [18], which may influence this cohort's poor participation in physical activities. In addition to breathlessness, psychological distress is common in patients with MPE. Psychological distress has been found to increase symptom burden and is associated with worse self-perceived health status [19], which may promote increased sedentary behaviours and cause patient apprehension to engage in physical activities. Another possible contributing factor to low physical levels in patients with MPE may be related to sarcopenia experienced by this cohort [20]. The relationship between symptoms and physical activity levels in patients with MPE is complex, and often multifactorial. Therefore, it is important to accurately measure physical activity levels in this cohort to provide clinically useful information which may guide supportive patient management.

Our findings show physical activity profiles of patients with MPE in Hong Kong are correlated to important domains of QoL. Increased sedentary behaviours were associated with less independence during self-care tasks, poorer mobility and worse overall health status. This indicates the importance of interventions aimed at increasing physical activity levels to potentially improve overall QoL in this cohort. Our group has shown the feasibility and benefit of an exercise training programme for patients with lung cancer to improve outcomes, including muscle mass, muscular strength, physical functioning and physical capacity [21]. Similar interventions may be beneficial to promote increased physical activity levels and QoL in patients with MPE.

Subjective patient and clinician reported measures of performance status, in particular the ECOG, are routinely measured for patients with cancer [22]. Performance status is commonly used to determine eligibility for oncology treatment (including chemotherapy) and eligibility to participate in clinical trials [23, 24]. Our data shows almost all participants reported a good performance status, suggesting they spend >50% of waking hours out of a chair or bed. This was not reflected in our objective findings as a proportion of participants' waking hours. Participants who reported a good performance status spent two-thirds of their waking hours sedentary, and less than a quarter of their waking hours performing light activities. However, there was a significant difference in the step count per day between good and bad performance status groups. These findings suggest performance status measures may not accurately measure the time patients spend engaging in activities of daily living. The practicality and accuracy of accelerometery supports its use as a favourable objective measure of activity behaviours.

This present study has limitations. The sample size was small, and most patients had lung cancer. Nonetheless the data provide a platform for future, larger, cross-sectional studies. The distribution of participant reported ECOG performance status was skewed towards patients with better functional status, a common issue as patients with advanced cancers with ECOG 3–4 are much less likely to partake in research studies. Another limitation is the number of participants who underwent chemotherapy treatment during the study period, which could have resulted in increased sedentary behaviours.

Conclusion

This is the first report of accelerometery-measured physical activity behaviours of patients with MPE in Hong Kong. Overall, participants spent the majority of their waking hours sedentary, which were related to poorer participation in self-care tasks. Therefore, accelerometery is a useful measure that correlates to important domains of QoL. Participants with good performance status spent 75% of waking hours sedentary, indicating a potential discrepancy between performance status measures and objective measures of activity levels in patients with MPE. Further studies are required to investigate whether changing physical activity in this population would increase QoL, and whether accelerometery accurately predicts survival in patients with MPE.

Provenance: Submitted article, peer reviewed.

Data availability: Deidentified individual participant data will be available to the scientific community with as few restrictions as possible while retaining exclusive use until publication of major outcomes. The statistical analysis plan is available upon reasonable request. Data requests from qualified researchers should be made to Y.C.G.L. (gary.lee@uwa.edu.au)

Ethics statement: The study was approved by the Institutional Review Board of the University of Hong Kong (#UW 17-516).

Author contributions: Y.C.G. Lee is the guarantor of this article. B.M. Iacopetta had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. B.M. Iacopetta, C.J. Peddle-McIntyre and Y.C.G. Lee contributed substantially to the study design, data analysis and interpretation,

and the writing of the manuscript. D.C.L. Lam, J.C.L. Ngai, J.W.M. Chan, F.K.Y. Chiang, M.M.S. Lui, W.L. Law, K.K.P. Chan and J. McVeigh contributed substantially to the study design and to the administration of the study, the acquisition of resources, data collection and analysis, and reviewing the final version to be published. All authors contributed data interpretation and have read and approved to the final approval of the manuscript.

Conflict of interest: The authors have reported that no potential conflicts of interest exist with any companies/organisations whose products or services may be discussed in the article.

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