The Burden of Specific Symptoms Reported by Survivors After Critical Illness

AJRCCM Articles in Press. Published on 26-June-2017 as 10.1164/rccm.201702-0398LE

RESEARCH LETTER

TITLE

The burden of specific symptoms reported by survivors after critical illness

CORRESPONDING AUTHOR

Dr David M Griffith MD, Senior Clinical Research Fellow, Anaesthesia, Critical Care and Pain Medicine, University of Edinburgh, Royal Infirmary of Edinburgh, 57 Little France Crescent, EH16 4SA.

Tel: 0131 242 6395

Email: david.m.griffith@ed.ac.uk

CO-AUTHORS

Dr Lisa Salisbury PhD,[1] Mr Robert J Lee MSc,[2] Dr Nazir Lone PhD,[3] Dr Judith L Merriweather PhD,[3] Professor Timothy Walsh MD,[3] On behalf of the RECOVER Investigators[3]

[1]School of Health Sciences, Queen Margaret University, Edinburgh, EH21 6UU, UK.

[2]Usher Institute for Population Health Sciences and Informatics, University of Edinburgh, Teviot Place, Edinburgh, EH8 9AG, UK.

[3]Anaesthesia, Critical Care and Pain Medicine, University of Edinburgh, Royal Infirmary of Edinburgh, 57 Little France Crescent, Edinburgh, EH16 4SA, UK.

Patients who survive critical illness sometimes report poor health-related quality of life (HRQoL)(1), but rehabilitation trials have mostly found no effect on this and other measures of health status (2–5). Most critical care research has employed tools such as the Medical Outcomes Study Short Form questionnaires (SF12/SF36) or EuroQol (EQ-5D) to measure HRQoL.(6) Although validated in general and other disease-defined cohorts, these generic patient-reported outcome measures may miss issues important to critical illness survivors. The use of specific symptoms associated with critical illness survivorship may improve our understanding of the burden of critical illness, and are not widely reported in the critical care literature (7).

In an ICU rehabilitation trial (RECOVER), we found no effect of the intervention on functional status, HRQoL and a range of other outcomes during 12 months follow-up (4). In a secondary analyses we aimed to describe trajectories of appetite, fatigue, pain, joint stiffness, and breathlessness symptoms that pre-trial pilot work identified as important to patients. We also aimed to examine the correlation between symptoms and generic HRQoL metrics.

As there were no inter-group differences in symptoms in the RECOVER trial, patients were analysed as a single cohort. Symptom data was available for 189/228 (83%), 166/220 (75%), and 161/218 (76%) of surviving patients at 3, 6, and 12 months respectively.

Symptoms (appetite, fatigue, pain, joint stiffness and breathlessness) were measured on a visual analogue scale (VAS) of 10cm in length ranging from 0 (no symptoms at all) to 10 (worse symptoms imaginable). Mean scores (and 95% confidence intervals) and frequency of patients with mild, moderate, and severe symptoms (scores of 0-3.3; 3.4-6.6; 6.7-10) were calculated at for each time point. Comparisons between 3 month symptoms and 12

AJRCCM Articles in Press. Published on 26-June-2017 as 10.1164/rccm.201702-0398LE

month symptoms for complete cases was made with paired t tests. Pearson correlation coefficients between symptoms and HRQoL (SF12v2 Physical Component Score (PCS) and Mental Component Score (MCS)) were calculated.

Symptom scores and severity category frequencies are shown in table 1. At ICU discharge fatigue and joint stiffness had the highest mean (standard deviation (SD)) scores (4.9(2.6) and 4.1(2.9) respectively) and more patients reported these symptoms as severe than other symptoms (30% and 25% respectively). Statistically significant improvements in pain, joint stiffness, and breathlessness were noted between 3 andd 12 months but clinically, these differences were small (less that a single centimetre on the VAS). At 12 months, there remained a significant proportion of patients experiencing symptoms at the most severe end of each symptom scale (table 1).

Symptoms correlated with PCS at 12 months (r (± 95% CI): appetite -0.37 (-0.23 to - 0.50), fatigue -0.61 (-0.69 to -0.52), pain -0.66 (-0.75 to -0.56), joint stiffness -0.64 (-0.73 to -0.54), breathlessness -0.44 (-0.57 to -0.30)) (table 2). Symptoms and MCS were also correlated, with strongest relationships observed for pain (-0·42 (-0.56 to -0.29)) and fatigue (-0·46 (-0.57 to -0.34)).

Previous investigators have shown that HRQoL is reduced following critical illness and that spontaneous improvement is limited, sometimes over many years (1). Some (but not all) rehabilitation trials have demonstrated improved functional outcomes, but have not necessarily improved HRQoL (4,5). In this analysis, we have shown that symptoms that influence daily life are prevalent following ICU discharge, are highly correlated with HRQoL, and frequently worsen in their severity over time.

Limitations of our study, include its small sample size (from one region of Scotland) which may limit generalisability to other healthcare settings. Whilst patients with missing data appeared similar at baseline, justifying the complete case approach, we cannot completely exclude bias arising from excluded patients. Finally, we were unable to assess effects of re-hospitalisation after critical illness which may have been more likely in multiply comorbid patients and could have contributed to ongoing symptoms.

Future research should consider including symptoms as outcome measures, since these may enrich the description of post-ICU health status.

The authors confirm that there are no conflicts of interest in relation to the submitted work.

Acknowledgements

This work was carried out on behalf of the RECOVER investigators: T S Walsh, L G Salisbury, J L Merriweather, J A Boyd, D M Griffith, G Huby, S Kean, S J Mackenzie, A Krishan, S C Lewis, G D Murray, J F Forbes, J Smith, J E Rattray, A M Hull, P Ramsay, C Wallis, J Stewart, A Bateman, E Wilson, M Gillies, D Hope, H Dawson, C McCulloch, J Antonelli, L Boardman, L Dow, W Williams, A McCann, S Alexander, J Norrie, M Dennis, C Waldmann and S Brett.

AJRCCM Articles in Press. Published on 26-June-2017 as 10.1164/rccm.201702-0398LE

References

1. Cuthbertson BH, Roughton S, Jenkinson D, MacLennan G, Vale L. Quality of life in the five years after intensive care: a cohort study. Crit Care. 2010;14(1):R6.

2. Denehy L, Skinner EH, Edbrooke L, Haines K, Warrillow S, Hawthorne G, et al. Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up. Crit Care. 2013;17(4):R156.

3. Moss M, Nordon-Craft A, Malone D, Van Pelt D, Frankel SK, Warner ML, et al. A Randomized Trial of an Intensive Physical Therapy Program for Patients with Acute Respiratory Failure. Am J Respir Crit Care Med. 2016 May 15;193(10):1101–10.

4. Walsh TS, Salisbury LG, Merriweather JL, Boyd JA, Griffith DM, Huby G, et al. Increased Hospital-Based Physical Rehabilitation and Information Provision After Intensive Care Unit Discharge: The RECOVER Randomized Clinical Trial. JAMA Intern Med. 2015 Apr 13;

5. Elliott D, McKinley S, Alison J, Aitken LM, King M, Leslie GD, et al. Health-related quality of life and physical recovery after a critical illness: a multi-centre randomised controlled trial of a home-based physical rehabilitation program. Crit Care. 2011;15(3):R142.

6. Lim WC, Black N, Lamping D, Rowan K, Mays N. Conceptualizing and measuring health-related quality of life in critical care. J Crit Care. 2016 Feb;31(1):183–93.

7. Black N. Patient reported outcome measures could help transform healthcare. BMJ. 2013 Jan 28;346:f167.

Table 1 – Symptom severity at 3, 6, and 12 months for all available patients. Measured by visual analogue scale 0-10 with 10 being most severe including appetite where 10 represents poorest appetite. Severity categories are mild (0-3.3); moderate (3.4-6.6) and severe (6.7-10). *For patients with data at both time points, mean of the paired differences (3-12 months) was calculated for each symptom. Paired t tests were used to compare the 3 and 12-month time points.

		3 months	6 months	12 months	Mean (95% CI) difference between 3 and 12 months*	P value*
APPETITE	n	188	166	157	155	
	Mean	3.6	3.4	3.4	0.2 (-0.2 to 0.7)	0.311
	SD	3.0	2.5	2.6		
	Mild	110 (59%)	97 (58%)	93 (59%)		
	Moderate	39 (21%)	49 (30%)	44 (28%)		
	Severe	39 (21%)	20 (12%)	20 (13%)		
FATIGUE	n	188	166	159	145	
	Mean	4.9	5.3	5.2	-0.3 (-0.8 to 0.1)	0.163
	SD	2.6	2.7	2.7		
	Mild	57 (30%)	40(20%)	49 (31%)		
	Moderate	74 (39%)	65 (39%)	55 (35%)		
	Severe	57 (30%)	61 (37%)	55(35%)		
PAIN	n	188	167	161	146	
	Mean	3.6	4.1	3.9	-0.5 (-1.0 to -0.1)	0.030
	SD	2.9	3.1	3.1		
	Mild	96 (51%)	71 (43%)	78 (48%)		
	Moderate	58 (31%)	52 (31%)	40 (25%)		
	Severe	34 (18%)	44 (26%)	43 (27%)		
JOINT STIFFNESS	n	188	167	156	143	
	Mean	4.1	4.6	4.8	-0.9 (-1.3 to -0.4)	<0.001
	SD	2.9	2.9	2.9		
	Mild	83 (44%)	64 (38%)	50 (32%)		
	Moderate	58 (31%)	52 (31%)	56 (36%)		
	Severe	47 (25%)	51 (31%)	50 (32%)		
BREATHLESSNESS	n	189	167	161	146	
	Mean	3.3	3.7	3.7	-0.6 (-1.0 to -0.1)	0.019
	SD	2.6	2.7	2.8		
	Mild	106 (56%)	81 (49%)	81 (50%)		
	Moderate	57 (30%)	59 (35%)	48 (30%)		
	Severe	26 (14%)	27 (16%)	32 (20%)		

AJRCCM Articles in Press. Published on 26-June-2017 as 10.1164/rccm.201702-0398LE

Table 2 – Pearson correlation between symptom scores and SF12 version 2 physical component score (PCS) and mental component score (MCS) at 3, 6 and 12 months. P values are 2 tailed. Abbreviations: n: sample size; r: Pearson's correlation coefficient.

		PCS			MCS		
		3 months	6 months	12 months	3 months	6 months	12 months
APPETITE	n	188	163	152	188	163	152
	r	-0.280	-0.328	-0.365	-0.317	-0.292	-0.299
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
FATIGUE	n	188	163	154	188	163	154
	r	-0.382	-0.522	-0.606	-0.435	-0.567	-0.457
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
PAIN	n	188	164	155	188	164	155
	r	-0.536	-0.580	-0.660	-0.343	-0.514	-0.419
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
JOINT STIFFNESS	n	188	164	151	188	164	151
	r	-0.377	-0.464	-0.643	-0.189	-0.375	-0.378
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
BREATHLESS	n	189	164	155	189	164	155
	r	-0.271	-0.374	-0.442	-0.323	-0.364	-0.293
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001