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Abbreviated title: Major Surgery & Quality of Life

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Number of Figures: 1

Number of Tables: 1

Word count: 612

MESH keywords: Surgery, Aging, Quality of Life

Key points:

Question: Is major surgery associated with changes in quality of life?

Finding: In this longitudinal prospective cohort study of 7,532 participants, surgery was associated with declines in physical, but not mental, quality of life. In contrast, medical admissions and the specific event of stroke exerted a larger effect, on both physical and mental quality of life.

Meaning: Major surgery is associated with only a small decrement in physical quality of life and this should be weighed against the potential overall health benefits of surgery.

Letter

While surgery can be life saving and prolonging, the impact on quality of life needs further investigation. Some studies suggest that surgery impacts both physical and mental function, while others emphasize impact on physical function alone[1,2]. Few studies have conducted prospective, long-term follow up, and no studies, to our knowledge, account for the pre-admission trajectory of physical and mental function. This is critical, as preoperative functional status influences the potential for improvement[3]. Furthermore, the sample size in these studies are typically small and focussed on single institutions or small groups of centers[4]. These limitations highlight the need for analysis of larger, longitudinal studies. Given our recent report of subtle cognitive decline after surgery[5], we aimed to clarify the effect of medical and surgical admissions on the trajectory of quality of life, considering both mental and physical function. As surgical and medical illnesses may cluster, it is important to consider the independent effects of each. We analyzed data from a prospective, longitudinal, population-based, cohort study linked to the United Kingdom healthcare record. We included data from 7,920 participants with up to five SF-36 quality of life assessments conducted between 1997 and 2016 in the Whitehall II study, with linkage to Health Episode Statistics registry for hospitalisation (**Supplemental Methods**). Exposures of interest included any "major" hospital admission, defined as requiring greater than one-night stay over the follow up. Stroke was included as a control to show changes were detectable. The primary outcomes were the mental (MCS) and physical (PCS) component score of the SF-36 quality of life scale. SF-36 composite scores reflect normalized (to reference population) points per event. Negative numbers indicate decreased quality of life. Bayesian linear mixed effects models were used to calculate the change in the quality of life trajectory following hospital admission. We also calculated the odds of substantial decline in

quality of life defined as >1.96 standard deviations from a predicted trajectory (based on the first three waves of data). Major surgery (n=1994) was associated with a decrease in PCS (-0.79 points, 95% Credible Interval [CI] -0.96 to -0.62), but not MCS (-0.10 points, 95% CI -0.28 to 0.08). Major medical admissions (n=765) were associated with decline in both PCS (-1.46 points, 95% CI -1.65 to -1.28) and MCS (-0.47 points, 95% CI -0.68 to -0.29, **Figure 1**). Notably while these changes were statistically significant, their effect sizes were substantially lower than that for stroke (**Table 1**) or the clinically significant change of five points[6]. The results were consistent across sensitivity analyses, including exclusion of emergencies, and in models including a variable for emergency surgery, that showed greater impairments in PCS (-0.91 (95% CI [-1.72, -0.08]), but not MCS (0.21 (95% CI [-0.67, 1.1]), for emergency than non-emergency procedures. For odds of substantial decline, major surgical (OR 1.80, 95% CI [1.28, 2.54]), medical (OR 2.24, 95% CI [1.48, 3.38]) or both types of admissions (OR 2.87, 95% CI [1.93, 4.32]) were associated with significant decline in PCS. However for MCS, only people with both medical and surgical admissions showed higher occurrence of substantial decline (OR 2.02 95% CI [1.31, 3.08]; surgical (OR 1.04, 95% CI [0.71, 1.51]; medical (OR 1.41, 95% CI [0.91, 2.18]) compared to those with no major admissions. Major medical admissions were associated with a decline in both mental and physical quality of life while major surgical admissions were only associated with changes in the physical components of quality of life. The average changes per admission were small, and while statistically significant, would not be considered clinically significant. Substantial impairments in quality of life are more likely for patients who incur both surgical and medical admissions.

Author Contributions: RDS and ASM conceived the study. BK, SS, HJM, ASM and RDS designed the study. BK analyzed the data with input from RDS, SS, HJM and ASM. BK and RDS wrote the paper with input from all authors. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Conflict of Interest Disclosures: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no competing interests that may be relevant to the submitted work.

Funding: RDS is supported by US National Institutes of Health (R01 AG063849-01 and R01 NS117901). The Whitehall II study is supported by grants from the US National Institutes of Health (R01AG056477, RF1AG062553), the UK Medical Research Council (MRC K013351, MR/R024227), and British Heart Foundation (RG/13/2/30098). SS is supported by the French National Research Agency (ANR-19-CE36-0004-01). The funder played no role in these analyses.

Additional contributions: We would like to thank Dr. Robert Bottle (Imperial College London) for advice on analysis and linkage of HES data.

Figure 1. Predicted quality of life trajectory before and after an admission event for a hypothetical average subject. Shaded region represent 95% credible intervals. Hypothetical admissions are demonstrated at the median age for first admission observed in the cohort analyzed. Variability due to random effects are omitted from credible intervals, so these intervals should be interpreted with respect to an average patient rather than across the population.

Table 1. Quality of life changes associated with surgery, medical admissions, stroke

Mental Composite Model [a]	β (95% CI)	p-value
Surgery (event) [b]	-0.10 (-0.28 to 0.08)	0.27
Medical (event) [b]	-0.47 (-0.68 to -0.29)	<0.001
Stroke (event) [b]	-1.28 (-2.83 to 0.28)	0.11
Surgery (baseline) [c]	-0.23 (-0.57 to 0.13)	0.19
Medical (baseline) [c]	-0.31 (-0.69 to 0.07)	0.12
Stroke (baseline) [c]	0.26 (-0.98 to 1.47)	0.68
# assessments [c]		
1	(ref)	
2	-0.59 (-1.41 to 0.24)	0.16
3	0.92 (0.16 to 1.71)	0.020
4	0.87 (0.16 to 1.59)	0.019
5	1.61 (0.98 to 2.29)	<0.001
Age	1.64 (1.50 to 1.77)	<0.001
Age^2	-1.13 (-1.24 to -1.03)	<0.001

Physical Composite Model [a]	β (95% CI)	p-value
Surgery (event) [b]	-0.79 (-0.96 to -0.62)	<0.001
Medical (event) [b]	-1.46 (-1.65 to -1.28)	<0.001
Stroke (event) [b]	-4.02 (-5.50 to -2.46)	<0.001
Surgery (baseline) [c]	-2.19 (-2.55 to -1.85)	<0.001
Medical (baseline) [c]	-2.10 (-2.50 to -1.72)	<0.001
Stroke (baseline) [c]	-0.98 (-2.23 to 0.25)	0.13
# assessments [c]		
1	(ref)	
2	0.80 (-0.07 to 1.59)	0.062
3	1.73 (0.97 to 2.52)	<0.001
4	2.36 (1.62 to 3.04)	<0.001
5	2.89 (2.25 to 3.55)	<0.001
Age	-2.42 (-2.54 to -2.28)	<0.001
Age^2	-0.75 (-0.85 to -0.66)	<0.001

[a] SF-36 composite scores are in normalized (to reference population with SD=10) units.
[b] Event-related coefficients reflect change per event. Negative numbers indicate decreased quality of life.
[c] Baseline adjustments apply equally to all study points for any given subject.

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