PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

Title (Provisional)

Understanding neurocognitive recovery in older adults after total hip arthroplasty: neurocognitive assessment, blood biomarkers, and patient experiences - a mixed methods study.

Authors

Amirpour, Anahita; Bergman, Lina; Markovic, Gabriela; Liander, Karin; Nilsson, Ulrica; Eckerblad, Jeanette

VERSION 1 - REVIEW

Reviewer	1
Name	Glumac, Sandro
Affiliation Intensive Care	Univ Hosp Split, Department of Anesthesiology and
Date	19-Sep-2024
COI	None

This study entitled "Understanding neurocognitive recovery in older adults after total hip arthroplasty: neurocognitive assessment, blood biomarkers, and patient experiences - a mixed methods study" seems to have been generally well executed and written. Furthermore, I believe that this paper will be of great interest to the readers and very educational. However, I have a few remarks that require authors attention, and a few suggestions to further improve the quality of this important work.

Abstract

Please provide a short Background of your study (1 to sentences) before the Objective.

Keywords

Consider some additional MeSH keywords (e.g., Neuropsychological Tests) to readers easier identify your research.

Introduction

Please state the clear hypothesis of your study at the end of Introduction.

Methods

Surgery and anesthesia

Please add this subsection in the Methods. Here, describe in brief how the surgery and anesthesia were performed.

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Zuo, Yunxia
Sichuan University, Anesthesiology
11-Oct-2024
None

This manuscript presents a mixed-methods study on postoperative neurocognitive recovery in older adults following total hip arthroplasty. It combines quantitative assessments of cognitive function and inflammatory biomarkers with qualitative patient interviews to provide a comprehensive view of the recovery process. The findings reveal that while few patients showed delayed neurocognitive recovery based on tests, many reported cognitive decline and fatigue, suggesting a disconnect between objective measures and patient experience. The study also indicates that psychological factors play a significant role in recovery outcomes.

Major comments

1. The manuscript mentions a sample size of 40 patients but does not provide the rationale behind this number, which is essential from a statistical perspective to ensure adequate power.

2. The exclusion criteria are listed, but there is no detail on how these criteria were applied, which could potentially lead to selection bias.

3. The absence of a control group, such as patients undergoing other types of surgeries or a similar group of patients not undergoing surgery, limits the comparability and generalizability of the results.

4. The manuscript mentions data analysis using SPSS but does not specify the exact statistical tests used or how the level of significance was determined.

5. For the integrated analysis of mixed-methods data, a clearer description of how quantitative and qualitative results were combined is needed.

6. The manuscript refers to tables and figures that are not included in the version reviewed. Ensure that all mentioned tables and figures are present in the final manuscript.

7. The limitations of the study and how they might affect the interpretation and generalizability of the results need to be discussed.

Minor comments

1. There are instances where research is discussed without a corresponding reference number, such as when discussing the impact of surgery type and anesthesia choices on POCD.

2. The conclusion should be concise and directly address the research objectives and hypotheses.

3. The reference formatting needs to be uniformly checked to ensure compliance with the journal's citation standards.

VERSION 1 - AUTHOR RESPONSE

1. This study entitled We thank you for the constructive and carefully considered feedback given to improve this manuscript. 1. This study entitled We thank you for the constructive and carefully considered feedback given to improve this manuscript. 1. This study entitled We thank you for the constructive and carefully considered feedback given to improve this manuscript.
"Understanding neurocognitive recovery in older adults after total hip arthroplasty: neurocognitive assessment, blood biomarkers, and patient experiences - a mixed methods study" seems to have
recovery in older adults after total hip arthroplasty: neurocognitive assessment, blood biomarkers, and patient experiences - a mixed methods study" seems to have
hip arthroplasty: neurocognitive assessment, blood biomarkers, and patient experiences - a mixed methods study" seems to have
assessment, blood biomarkers, and patient experiences - a mixed methods study" seems to have
patient experiences - a mixed methods study" seems to have
methods study" seems to have
been generally well executed and
written. Furthermore, I believe
that this paper will be of great
interest to the readers and very
educational. However, I have a few
remarks that require authors
attention, and a few suggestions to
further improve the quality of this
important work.
2. Abstract This has been added to the Abstract, page 2
Please provide a short Background row 25-29.
of your study (1 to sentences) Objective: Delayed neurocognitive
before the Objective. recovery, previously known as postoperative
cognitive dysfunction, is a common
complication affecting older adults after
surgery. This study aims to address the
knowledge gap in postoperative
relationship between subjective exploring the
nerformance based manufacture experiences,
blood biomarkers
biobu biolitarkers.

3.	Keywords Consider some additional MeSH	We have updated the keywords to MeSH keywords. Page 2, row 51-52
	keywords (e.g.,	
	Neuropsychological Tests) to	"Keywords: arthroplasty, replacement, hip,
	readers easier identify your	neurocognitive disorders,
	research.	neuropsychological tests, postoperative
	T / T /•	cognitive complications
4.	Introduction	This has been added, page 4, row 112-113.
	Please state the clear hypothesis of	"We have the size of the tractice to showing a
	your study at the end of Introduction	dealing in performance based tests would
		report differing experiences in the
		interviews and vice versa "
5	Methods	We appreciate the suggestion of adding
	Surgery and anesthesia	surgery and anesthesia details. The total hip
	Please add this subsection in the	arthroplasty was carried out according to
	Methods. Here, describe in brief	normal clinical practice. Since outcome
	how the surgery and anesthesia	related to surgical technique is not part of
	were performed.	this study's outcomes, we have not
	-	expanded this section further.
		This has been added and revised, page 7,
		row 196-202
		"Surrowy and an asthasia
		"The total hip arthroplasty surgery was
		carried out in accordance with normal
		clinical practice Patients received spinal
		anesthesia either with 0.25 ml morphine (0.4
		mg ml) and 2.8 ml bupiyacaine (5 mg ml) at
		level L3–L4 or L2-L3, or with 3.5 ml
		bupivacaine (5 mg ml) only. Four patients
		underwent general anesthesia with tracheal
		intubation, using a combination of induction
		drugs such as Alfentanil, Propofol, Fentanyl
		and a variation of neuromuscular blocking
		drugs, and maintenance anesthesia with
		Sevoflurane."
D •		
Keviev 1	This manuscript proceeds a minut	Kesponses and comments
1.	methods study on postonorative	carefully considered feedback given to
	neurocognitive recovery in older	improve this manuscript
	adults following total him	
	arthronlasty. It combines	
	an antipative assessments of	
	cognitive function and	
	inflammatory biomarkers with	
	qualitative patient interviews to	
	provide a comprehensive view of	
L	· · · · · · · · · · · · · · · · · · ·	1

-		
the recovery proce	ess. The findings	
reveal that while f	ew patients	
showed delayed no	eurocognitive	
recovery based on	tests, many	
reported cognitive	decline and	
fatigue, suggesting	y a disconnect	
between objective	measures and	
natient experience	The study also	
indicatos that new	shological factors	
nucates that psyc	nolo in nonovony	
play a significant	role in recovery	
outcomes.		
2. The manuscript m	ientions a sample	Since this is a mixed methods study, the
size of 40 patients	but does not	main purpose is to gain new knowledge
provide the ration	ale behind this	about the concept delayed neurocognitive
number, which is	essential from a	recovery – rather than drawing statistical
statistical perspec	tive to ensure	conclusions. This is also why the study is
adequate power.		QUAL+quan, meaning, qualitatively
		dominant in its interpretations and findings.
		1 0
		The sample was made as a convenience
		sampling We did not perform a formal
		sample size calculation. The sample size
		sample size calculation. The sample size
		was determined at the time of when the
		study protocol was written (in 2019) and
		based on the earlier classification of
		postoperative cognitive dysfunction (POCD)
		and incidence of 17-25% (Silbert et al,
		Anesthesiology 2015).
		We have updated the methods section, page
		5, row 133-134.
		"Between October 2019 and November
		2021, we included 40 patients aged ≥ 60
		years through convenience sampling,
		dropouts were 6 patients (Figure 1)."
		And the discussions section, page 17, row
		496-500
		"We acknowledge the limitations of this
		study Limitations include strict eligibility
		criteria which led to the evolution of many
		notionta and may have evolved freiler
		patients, and may have excluded fraher
		individuals, e.g., those with nervous system
		diseases. Generalizability of our results is
		limited due to small number of participants
		and subjective reports. The convenience
		sampling is also a limitation."
3. The exclusion crit	eria are listed,	We have added this detail to the manuscript
but there is no det	ail on how these	page 5, row 135-136

		1
	criteria were applied, which could potentially lead to selection bias.	"All potential eligible study participants were preliminary screened and approached
		by the fourth author."
4.	The absence of a control group, such as patients undergoing other types of surgeries or a similar group of patients not undergoing	We acknowledge the limitation of not having a surgical control group. However, the neurocognitive test results were matched with a nonsurgical control group
	surgery limits the comparability	
	and generalizability of the results	(See Data analysis – statistical analysis)
		As this is a mixed methods study, the main purpose is not to draw generalizations but to enhance understanding and breadth of the phenomenon delayed neurocognitive recovery after surgery. This is why we applied the mixed methods design.
5.	The manuscript mentions data	We have specified the exact tests in
	analysis using SPSS but does not	manuscript, page 7, row 211-222
	specify the exact statistical tests	"Statistical analysis
	used or how the level of	Descriptive statistics are presented as means.
	significance was determined	standard deviations, median score, and
	Significance was accordinated	completion times for the neurocognitive test
		battery Wilcoxon signed rank test was
		applied to assess changes in raw scores and
		completions times for the neurocognitive
		tost hottomy Normality of the date was
		test battery. Normanity of the data was
		assessed with Q-Q plots, instograms and
		Shapiro wilk lest. A two-sided p-value of
		<0.05 was considered as statistically
		significant. Cognitive performance changes
		were adjusted for practice effects and
		variability using age-matched nonsurgical
		controls, the z-scores were calculated to
		assess changes from preoperative to
		postoperative tests with dNCR defined as a
		z-score of ≥ 1.0 on day 13-16 after surgery,
		z-score of <1.0 on day 13-16 indicated no
		decline according to the ISPOCD method
		we followed the diagnostic rule for delayed
		at least two sub tests We used IDM SDSS
		at reast two sub-resis we used IDIVI SPSS
		statistical analysis "
		statistical allalysis.
6	For the integrated analysis of	We have edited and added this information
υ.	rui une integrateu analysis ui mixad-mathada data a alaanan	in the manuscript page 8 row 220 246
	description of how quantitative	In the manuscript, page o 10w 239-240
	and qualitative results were	"All findings were discussed within the
	and quantative results were	research group. The initial proposed display
		research group. The initial proposed display

7. The manuscript refers to tables and figures that are not included in the version reviewed. Ensure that all mentioned tables and figures are present in the final manuscript	was created by AA through an iterative process, with patterns, revisions and reviews conducted by LB and GM. " We have double-checked the entire manuscript. In the manuscript, there is Figure 1 and Table 1-3 in this manuscript, each figure and table are referred to in-text. We also have supplementary material 1 and 2 and mentioned this in the manuscript as well.
8. The limitations of the study and how they might affect the interpretation and generalizability of the results need to be discussed.	We have updated the discussions section: Page 17 row 496-505 "We acknowledge the limitations of this study. This include strict eligibility criteria which led to the exclusion of many patients, and may have excluded frailer individuals, e.g., those with nervous system diseases. Generalizability of our results is limited due to convenience sampling and a small number of participants. Further,-this study lacked a standardized delirium assessment while patients were at the hospital and a preoperative depression screening. However, the SwQoRdoes include items assessing anxiety and depressive symptoms. While we acknowledge the potential for bias with the same person conducting both tests and interviews, efforts were made to minimize bias by standardizing the test procedure and instructions provided to all participants."
9. There are instances where research is discussed without a corresponding reference number, such as when discussing the impact of surgery type and anesthesia choices on POCD	We have double-checked the manuscript and updated the references where needed.
10. The conclusion should be concise and directly address the research objectives and hypotheses.	The conclusion has been revised: Page 18 row 511-517 "We found a disparity between subjective reports of neurocognitive recovery and performance-based measurements. Only five patients were classified as having delayed neurocognitive recovery, however many

	patients described changes in their daily functioning due to cognitive and psychological symptoms. Our study highlights the complexity and breadth of postoperative neurocognitive recovery which extends beyond psychometric testing and blood samples. "
11. The reference formatting needs to be uniformly checked to ensure	We have updated the references according to the journal's standards.
compliance with the journal's citation standards.	