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Short communication

Delirium and long-term psychopathology following surgery in older adults

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ABSTRACT

Objective: To describe the risk of postoperative delirium and long-term psychopathology (depression, anxiety or post-traumatic stress syndrome (PTSS)) in older adults.
Methods: 255 elderly patients (≥ 65 years) undergoing major surgery (planned surgical time > 60 min) in a tertiary hospital were compared to 76 non-surgical controls from general practice. Patients were assessed twice daily for postoperative delirium using the Confusion Assessment Method (CAM(-ICU)), nursing delirium screening scale (NuDESC) and validated chart review. Before surgery and 3 and 12 months thereafter, the participants filled in the Hospital Anxiety and Depression Scale (HADS), the Geriatric Depression Scale (GDS-15) and the Post-Traumatic Stress Syndrome-14-Questions Inventory (PTSS-14). Non-surgical controls filled in the same questionnaires with similar follow-up.
Results: Patients were more often male, had higher American Society of Anesthesiologists scores and more often had a spouse compared to controls ($p < 0.005$). Forty-three patients (18%) developed postoperative delirium, who were significantly older, had higher ASA scores and lower estimated IQ scores compared to the patients who did not develop delirium ($p < 0.05$). There were no differences in psychopathology at baseline and 3-month follow-up between patients and controls. At 12-months, surgical patients less frequently scored positive for depression (7% versus 16%) and anxiety (2% versus 10%) compared to nonsurgical controls ($p < 0.05$). We did not observe differences in occurrence of psychopathology between patients who had and had not developed postoperative delirium.
Conclusion: Our results suggest that the older surgical population, with or without postoperative delirium, does not appear to be at greater risk of developing psychopathology.
Why does this paper matter?: The older surgical population does not appear to be at greater risk of developing psychopathology, neither seems this risk influenced by the occurrence of postoperative delirium

1. Introduction

By the year 2050, an estimated 16% of the global population will be older than 65 years, in contrast to 9% in 2019 [1,2]. This rapid rate of population aging is accompanied, or even outpaced, by an increase in the number of older adults who need surgery [3]. Although elective surgery is generally safe, it is not without risk [4]. Moreover, the rate of postoperative mortality, overall morbidity and postoperative complications increases with age [5]. Several questions regarding long-term postsurgical outcomes in older adults, however, remain unclear. The most common psychiatric disorders in the European elderly are mood disorders and anxiety, with an estimated 12-month incidence of 14% respectively 17% [6]. In the Netherlands, the prevalence of mood disorders (depression and dysthemia) is 2–5% and that of anxiety disorders 10% [7]. Whereas anxiety, depression and post-traumatic stress syndrome (PTSS), which we will refer to as psychopathology in the current study, are common after Intensive Care Unit (ICU) admission [8–10], previous studies have reported contradicting results on psychopathology

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following surgery [11–19]. These mixed findings may be due to the influence of other postoperative conditions, such as delirium. Therefore, the aim of this study was two-fold: 1) to report the incidence of psychopathology in surgical and nonsurgical patients at baseline and 3- and 12-months thereafter to gain insight in its occurrence and development over time, and 2) to determine whether the relationship between surgery and psychopathology differs by the onset of postoperative delirium.

2. Methods

We prospectively included non-demented patients ≥65 years, undergoing major elective surgery in our tertiary hospital (University Medical Center Utrecht) in the Netherlands. Major elective surgery was defined as orthopedic-, cardiac-, gastro-intestinal-, maxillofacial- or otolaryngological surgery with planned surgery time ≥ 60 min. Possible dementia was defined as a Mini-Mental State Evaluation (MMSE) ≤ 23, intelligence quotient (IQ) was estimated using the National Adult Reading Test. In addition, we recruited nonsurgical controls from a general practitioner's office in Utrecht, the Netherlands using the same in- and exclusion criteria and based on the age distribution among the patients. The control subjects were not scheduled for surgery in the upcoming 12 months. All participants signed informed consent and all procedures were approved by the local medical ethics committee (protocol 14–469).

2.1. Delirium assessment

In the seven days following surgery, or until discharge, trained researchers used a validated chart review [20], the Confusion Assessment Method (CAM(-ICU)), and the nursing delirium screening scale (NuDESC) twice daily to assess delirium [21]. Delirium was considered present in case of a positive CAM(-ICU) or ≥ 2 cumulative points on the NuDESC and/or patient chart review that showed predefined descriptions.

2.2. Long-term psychopathology

Participants filled in questionnaires concerning psychopathology at baseline and 3- and 12-month follow-up. The baseline visit took place prior to surgery, ranging from the day before surgery to two weeks before surgery. The questionnaires included the 15-item Geriatric Depression Scale (GDS-15), the Hospital Anxiety and Depression Scale (HADS) and the Post-Traumatic Stress Syndrome-14-Questions Inventory (PTSS-14). The latter was only filled in by the patients at 3- and 12-month follow-up, the 3-month questionnaire also inquired about preoperative PTSS symptoms.

The HADS is divided into a depression and an anxiety subscale, respectively the HADS-D and HADS-A. Possible depression was defined as >5 points on the GDS-15 and/or ≥ 8 points on the HADS-D, possible anxiety as ≥8 points on the HADS-A and possible PTSS as ≥45 points on the PTSS-14 [22–24]. A positive score on either depression, anxiety and/or PTSS was considered psychopathology.

2.3. Statistical analysis

Continuous variables were compared between patients and controls, or between the delirium and the non-delirium group using either a two-samples *t*-test or Mann-Whitney *U* test, whichever was appropriate. Differences in categorical variables were compared using either Fisher's exact test or chi-square test. Differences in ordinal variables (questionnaire outcomes) were compared using Kruskal Wallis test. In case of missing observations, comparisons were based on available case analysis.

3. Results

A total of 255 patients and 79 nonsurgical controls were included. Three control subjects were excluded because they underwent a surgical procedure during follow-up, resulting in 76 nonsurgical controls available for analysis. In 11 out of 255 patients (4%), delirium status could not be assessed due to logistic reasons. In the remaining 244 patients, delirium occurred in 43 cases (18%). Surgical patients had a higher proportion of males, had higher ASA scores and more often lived with a partner. Surgical patients that developed delirium were significantly older, had a higher ASA score, a lower estimated IQ, underwent more cardiothoracic surgery, were more often admitted to the ICU and had longer hospital length of stay compared to patients who did not develop delirium (Table 1).

There were no differences in preoperative psychopathology between patients and controls. In the delirium group, the percentage of patients with baseline anxiety symptoms was higher compared to the non-delirium group, although not statistically significantly (5% versus 0.5%, $p = 0.083$).

Twenty-five patients and 4 controls were lost to follow-up and excluded. Patients lost to follow-up had significantly higher ASA scores, higher BMI, lower IQ and longer hospital duration of stay than patients that were not lost to follow-up. The were no differences at baseline between nonsurgical controls that were lost to follow-up and controls that were not.

There were no differences between surgical patients and nonsurgical controls at 3-month follow-up. At 12-month follow-up, less patients scored positive for depression (7% versus 16%, $p = 0.036$) and anxiety (2% versus 10%, $p = 0.023$) compared to the nonsurgical controls. This difference was also reflected in the median HADS-D and HADS-A scores, which were significantly lower in the patient group compared to the control group (median HADS-D 4 [Interquartile range (IQR) 2–6] versus 6 [IQR 5–8], $p < 0.0001$, and median HADS-A 3 [IQR 2–5] versus 4 [IQR 2.5–6], $p = 0.002$).

Surgical patients who had developed delirium had higher GDS-15 scores at 3- and 12-month follow-up compared to patients who had not (3-month follow-up: median score 2 [IQR 0–3] versus 1 [IQR 0–2], $p = 0.037$, 12-month follow-up: median score 4 [IQR 3–4] versus 3 [IQR 2–5], $p = 0.005$). However, the clinically significant threshold was not exceeded in any case resulting in no statistically significant differences in occurrence of depression, anxiety and PTSS symptoms at both 3- and 12-month follow-up between patients who developed postoperative delirium and those who did not.

4. Discussion

In summary, we observed the highest prevalence of depressive and anxiety symptoms at 12-month follow-up. In the nonsurgical control group the prevalence of depressive and anxiety symptoms was respectively 16 and 10%. In the surgical group this was 7% for depressive symptoms and 2% for anxiety symptoms. There was no significant difference in the occurrence of psychopathology between surgical patients that developed delirium in the postoperative period and those who did not.

This incidence of depressive symptoms found in the nonsurgical controls (16%) is comparable to the 12-month incidence reported in Europe (14%), while the incidence of anxiety symptoms is lower in our study population (10%) compared to the European incidence (17%) [6]. In the Netherlands, however, mood disorders are reported in 5% of older adults and anxiety disorders in 10%, the latter being more comparable to the results found in our study [7]. The higher incidence of depressive symptoms can be explained by the usage of questionnaires to screen for depressive symptoms, which might result in an overestimation of actual depressive disorders. The incidence of psychopathologpy in the patient group is lower than expected. In the literature, reported incidence of postoperative depressive symptoms ranges from 8 to 44% for different

Table 1
– Baseline differences between groups.

Variable	Surgical patients			Nonsurgical Controls ($n = 76$)
	Delirium+ ($n = 43$)	Delirium- ($n = 201$)	Total ($n = 255$)	
Sex (n(%))				
Male[b]	27 (63%)	141 (70%)	175 (69%)	38 (50%)
Female	16 (37%)	60 (30%)	80 (31%)	38 (50%)
Age (median (IQR))[d]	73 (71–77)	70 (68–74)	70 (68–74)	71 (67–76)
BMI (median (IQR))	26.2 [24.1–28]	26.5 [24.1–29]	26.5 [24–29]	25.9 [24.4–28.5]
ASA classification (n (%))[b,d]				
ASA I	0 (0%)	22 (11%)	23 (9%)	21 (28%)
ASA II	18 (42%)	114 (57%)	136 (53%)	36 (47%)
ASA III	25 (58%)	65 (32%)	96 (38%)	19 (25%)
Type of surgery (n(%))[d]				
Cardiothoracic	22 (51%)	47 (23%)	72 (28%)	n.a.
Orthopedic and spine	9 (21%)	57 (28%)	67 (26%)	n.a.
Gastro-intestinal surgery	7 (16%)	19 (10%)	27 (11%)	n.a.
Urogential	2 (5%)	44 (22%)	48 (19%)	n.a.
Head and neck	3 (7%)	34 (17%)	41 (16%)	n.a.
Premorbid IQ (median (IQR))*[c]	101 [92–109]	106 [97–113]	106 [97–113]	107 [99–115]
MMSE score (median (IQR))**	28 [27–30]	29 [28–30]	29 [28–30]	29 [28–30]
Living situation:[b]				
Alone	7 (16%)	42 (21%)	56 (22%)	31 (41%)
With partner	36 (84%)	147 (73%)	186 (73%)	43 (57%)
Other	0 (0%)	2 (1%)	2 (1%)	1 (1%)
Unknown	0 (0%)	10 (23%)	11 (4%)	1 (1%)
Hospital Length of Stay (days (median (IQR)))***[d]	9 [7–13]	3 [2–6]	4 [2–8]	n.a.
ICU admission (n(%))***[d]	21 (53%)	40 (21%)	62 (26%)	n.a.
ICU Length of Stay (days (median (IQR))***	1 [1–1]	1 [1–1]	1 [1–1]	n.a.
Depression - Baseline				
Response rate	*43 (100%)*	*196 (98%)*	*250 (98%)*	*76 (100%)*
Baseline depression symptoms				
Positive (n(%))	1 (2.5%)	2 (1%)	3 (1%)	2 (2.5%)
Baseline HADS-D score (median (IQR))	2 [1–3]	2 [1–4]	2 [1–4]	3 [1–4]
Baseline GDS-15 score (median (IQR))	1 [0–2]	1 [0–2]	1 [0–2]	1 [0–2]
Anxiety – Baseline				
Response rate	*43 (100%)*	*198 (99%)*	*252 (99%)*	*76 (100%)*
Baseline anxiety symptoms				
Positive (n(%))	2 (5%)	1 (0.5%)	3 (1%)	2 (3%)
Baseline HADS-A score (median (IQR))	3 [1–4]	3 [1–4]	3 [1–4]	3 [2–4]
PTSS – Baseline				
Response rate	*29 (67%)*	*175 (87%)*	*208 (82%)*	*n.a.*
Baseline PTSS symptoms				
Positive (n(%))	0 (0%)	1 (0.5%)	1 (0.5%)	n.a.
Baseline PTSS-14 score (median (IQR))	14 [12–19]	13 [11.8–16]	13 [12–16]	n.a.

Findings are either presented as numbers(%) or median [interquartile range]. Surgical patients are both presented as group as a whole, and stratified for the presence or absence of postoperative delirium. Since for 11 surgical patients it is not known whether they developed delirium, these patients are only represented in the surgical patients (total) group. In 7 of these patients, delirium could not be assessed because the patient was already discharged before measurements could take place, and electronic health records were either inconclusive or the chart was not filled out. For 4 patients, chart review was carried out and indicated no delirium, but CAM and NuDESC were missing. *Premorbid IQ was missing in 10 patients, of which 2 were missing in the delirium group, 7 in the no-delirium group and the remaining one in the group with unknown delirium status. **MMSE was missing in 37 surgical patients and 4 nonsurgical controls. Within the patient group, MMSE was missing in 10 subjects in the delirium group and 20 in the non-delirium group. The remaining 7 missing MMSE scores were in the delirium-unknown group. ***information on hospital and ICU length of stay was missing in respectively 16 and 15 patients, both were missing in 3 in the delirium group, 6 in de non-delirium group and respectively 7 and 6 in the remaining group with unknown delirium status. [a]$p < 0,05$ patients versus controls; [b]$p < 0,005$ patients versus controls; [c]$p < 0,05$ delirium versus non-delirium; [d]$p < 0,005$ delirium versus non-delirium. Abbreviations: BMI (Body Mass Index), ASA (American Society of Anesthesiologists), IQ (Intelligence Quotient), MMSE (Mini-Mental State Evaluation), HADS (hospital anxiety and depression scale), GDS (geriatric depression scale), PTSS (post-traumatic stress syndrome).

follow-up durations and a wide range of surgical procedures [11,12,14,16,25]. The lower incidence found in our study may be attributed to the accessible consultation of geriatric specialists in our hospital, who are standardly involved in the perioperative care of all patients >70 years. Moreover, the response rate to the questionnaires might have underestimated the measured incidence of psychopathology in the current study, which was slightly higher in the control group and had the lowest response in patients who had been delirious (Table 2). Patients that were lost to follow-up had higher ASA scores, higher BMI and lower estimated IQ compared to patients that were not lost to follow-up. These patients may have been at higher risk of psychopathology than patients who completed follow-up. In addition, female sex and living alone appears to increase the risk of psychopathology [26]. In our cohort, controls were significantly more often female and lived more often alone than the patients. Due to the small number of patients developing symptoms, we had insufficient power to correct for these confounding factors.

Patients developing delirium were significantly older and had higher ASA scores than patients who had not developed delirium, which is in line with previous literature in which age and comorbidity were found to increase the risk of postoperative delirium [27–29]. Although psychiatric disorders, especially depression, are also reported as risk factors for postoperative delirium, this could not be confirmed although preoperative anxiety symptoms were more frequent in the group developing delirium (however not statistically significant, $p = 0.083$) [27–29]. In addition, it is presumed that postoperative delirium is associated with long-term psychopathology, especially PTSS [17,29–31]. We could not confirm this association in the current study.

This is the first study on long-term psychopathology following major surgery in the elderly, using an age-matched control group of nonsurgical elderly. This makes it possible to control for neuropsychiatric disorders that emerge in this age group regardless of surgery. Another strength of this study is that we assessed whether postoperative delirium occurred and that participants were followed for 12 months, which enabled studying the emergence and/or possible disappearance of psychopathology over time.

Our study also has several limitations. First, there were significant baseline differences between groups that may explain the lower incidence of psychopathology found in our patient group, for which we were unable to adjust due to insufficient power.

Second, we used the ASA-score as a proxy for comorbidity and therefore we cannot rule out that certain comorbidities that are known to increase the risk of psychopathology (such as cancer or premorbid chronic pain) have influenced our results. Since nonsurgical controls were more often ASA1, while exhibiting a higher incidence of psychopathology, we expect that this influence was minimal.

Third, we did not assess delirium severity which may be a more important predictor of poor long-term outcomes than delirium incidence.

Finally, missing data exceeded 10% for some outcome variables, with significant differences between patients that were lost to follow-up and those who were not. This could have resulted in selection bias possibly underestimating the incidence of psychopathology in the surgical group.

Table 2
– Psychopathology at 3- and 12-month follow-up.

Variable	Surgical patients			Nonsurgical Controls ($n = 72$)
	Delirium+ ($n = 37$)	Delirium- ($n = 189$)	Total ($n = 230$)	
Depression – 3 months				
Response rate	*32 (74%)*	*189 (94%)*	*221 (88%)*	*72 (95%)*
Depression symptoms				
Positive (n(%))	0 (0%)	1 (0.5%)	2 (1.0%)	1 (1.5%)
HADS-D score (median (IQR))	2 [1–6]	1 [1–4]	2 [1–4]	2 [1–4]
GDS-15 score (median (IQR))[c]	2 [0–3]	1 [0–2]	1 [0–2]	1 [0–2]
Anxiety – 3 months				
Response rate	*32 (74%)*	*187 (93%)*	*223 (88%)*	*72 (95%)*
Anxiety symptoms				
Positive (n(%))	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)
HADS-A score (median (IQR))	3 [0–4]	2 [1–3]	2 [1–3]	2 [1–4]
PTSS – 3 months				
Response rate	29 (67%)	175 (87%)	208 (82%)	
PTSS symptoms				
Positive (n(%))	0 (0%)	1 (0.5%)	1 (0.5%)	n.a.
PTSS-14 score (median (IQR))	19 [15–24]	17 [15–20]	17 [15–21]	n.a.
Depression – 1 year				
Response rate	33 (77%)	164 (82%)	200 (78%)	62 (82%)
Depression symptoms				
Positive (n(%))[a]	3 (9%)	10 (6%)	13 (7%)	10 (16%)
HADS-D score (median (IQR))[b]	5 [2–6]	4 [2–6]	4 [2–6]	6 [5–8]
GDS-15 score (median (IQR))[d]	4 [3–4]	3 [2–4]	3 [2–4]	3 [2–4]
Anxiety – 1 year				
Response rate	33 (77%)	169 (84%)	205 (80%)	63 (83%)
Anxiety symptoms				
Positive (n(%))[a]	0 (0%)	5 (3%)	5 (2%)	6 (10%)
HADS-A score (median (IQR))[b]	4 [3–4]	3 [2–5]	3 [2–5]	4 [2.5–6]
PTSS – 1 year				
Response rate	32 (74%)	167 (83%)	202 (79%)	
1 Year PTSS symptoms				
Positive (n(%))	0 (0%)	1 (0.5%)	1 (0.5%)	n.a.
1 Year PTSS-14 score (median (IQR))	21 [16–30]	19 [15–24]	19 [16–24]	n.a.

Findings are either presented as numbers (%) or median [interquartile range]. Of 25 surgical patients and 4 controls, follow-up data was missing and therefore these participants were excluded from further analysis on long-term psychopathology. Of the 230 surgical patients included in the analysis, 37 were patients that had developed delirium and 189 were patients that had not developed delirium. Of 4 surgical patients, delirium status was unknown. For these patients, chart review had been filled in as 'no delirium', but NuDESC and CAM were missing. [a]$p < 0{,}05$ patients versus controls; [b]$p < 0{,}005$ patients versus controls; [c]$p < 0{,}05$ delirium versus non-delirium; [d]$p < 0{,}005$ delirium versus non-delirium. Abbreviations: HADS (hospital anxiety and depression scale), GDS (geriatric depression scale), PTSS (post-traumatic stress syndrome).

5. Conclusion

Our study results suggest that the older surgical population does not appear to be at greater risk of developing psychopathology, neither seems this risk influenced by the occurrence of postoperative delirium. However, to fully disprove an association, prospective studies that are sufficiently powered to correct for important baseline variables should be undertaken.

Author contributions

The original study was designed by A.J.C.S. Acquisition of subjects and data collection was performed by I.M.J.K. and S.J.T.M. The current research question and study design was worked out by N.M., A.J.C.S., O. L.C. and W.J.M.S. The data was prepared by M.E.C.B. and N.M. Data-analysis was performed by N.M. The manuscript was prepared by N. M. and M.E.C.B. and finalized by N.M. and A.J.C.S. The manuscript was revised by all co-authors.

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Declaration of Competing Interest

The authors have no conflicts of interest.

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