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Association between selective serotonin reuptake inhibitors use and blood transfusion risk in older adults after hip fracture: a cohort study

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Abstract

Background Hip fracture is common and associated with high morbidity and mortality rates. Selective serotonin reuptake inhibitors (SSRIs) influence platelet hemostasis and might result in abnormal bleeding. This study aims to determine whether the use of SSRIs in older patients undergoing hip fracture surgery is associated with the risk of perioperative red blood cell (RBC) transfusion.

Methods We conducted a retrospective observational study using prospectively collected data of patients aged 70 years and older admitted to a French geriatric perioperative ward for hip fracture between January 2012 and June 2021. The primary endpoint was the occurrence of RBC transfusion during hospitalization. Multivariate logistic regression was performed, with a sensitivity analysis according to co-prescriptions.

Results Out of 1085 patients, 253 (23%) were male, mean age was 86 (±6.2) years, and median Charlson Comorbidity Index was 7 (interquartile range [5–8]). 486 (45%) patients received perioperative RBC transfusion, with a median of 2 units (interquartile range [1–3]) transfused per patient postoperatively. After adjusting for age, sex, comorbidities, functional status, institutionalization, polypharmacy, antiplatelet therapy, fracture type, hemoglobin and albumin levels, the use of SSRIs was not associated with an increased risk of RBC transfusion (aOR 0.91, 95%CI 0.64–1.29, $p=0.59$). We did not observe any association between concomitant use of SSRIs and anticoagulant or antiplatelet therapy and the risk of RBC transfusion.

Conclusions Among older comorbid adults undergoing hip fracture surgery, the use of SSRIs was not associated with an increased risk of perioperative RBC transfusion.

Keywords Hip fracture, Red blood cell transfusion, Selective serotonin reuptake inhibitors, Orthogeriatric pathway, Platelet hemostasis, Perioperative

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Background

Hip fracture is a common and serious issue in older adults. Its worldwide global incidence is expected to reach 4,5 million by 2050 [1]. It is associated with increased morbidity, and 6-month mortality which can reach up to 23% after hip fracture surgery [2]. Postoperative complications are frequent, and adversely affect outcomes of older patients undergoing hip fracture surgery, notably perioperative blood transfusion being associated with increased 6-month mortality [3]. Hemorrhagic complications such as surgical hematoma, anemia, and red blood cell (RBC) transfusion are common after hip fracture surgery. RBC transfusion is required in up to 30% of patients after hip fracture surgery [4]. Older age, comorbidities, and anticoagulant use are associated with an increased risk of RBC transfusion after hip fracture surgery [5–8]. Older patients are also more likely to be treated with anticoagulants and antiplatelet agents, particularly those with cardiovascular diseases [9–11].

Selective serotonin reuptake inhibitors (SSRIs) are used for major depressive and anxiety disorders [12] and are commonly used among older patients [13], where the prevalence of depression can reach 15% in patients over 85 years [14]. Serotonin is involved in platelet activation [15]. Once taken up from plasma and stored in platelet granules, it can be released into the blood during the early phases of platelet aggregation [16]. Although serotonin is a weak platelet activator, SSRIs affect platelet hemostasis, by decreasing platelet activation and aggregation, further leading to abnormal bleeding [16, 17]. An association has been reported between SSRI use and increased risk of gastrointestinal bleeding [17, 18], intracranial hemorrhage [17], and hematuria [19]. The bleeding risk is increased with concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) [18], antiplatelet therapy and anticoagulants [20].

In the perioperative setting, the use of SSRIs is also associated with an increased risk of bleeding and RBC transfusion [21–24], even in combination with antiplatelet agents [18]. However, these studies focused on patients of all ages undergoing all kinds of orthopedic surgery, without specifically examining outcomes in patients aged 70 years and older after hip fracture surgery.

The aim of this study was to determine whether hospitalized patients treated with SSRIs have a higher risk of RBC transfusion after hip fracture surgery.

Methods

The database was declared to the French National Commission on Computing and Liberty (CNIL) of Assistance Publique-Hôpitaux de Paris (AP-HP) (n° 20190426181554). Data was collected as part of routine care, with the possibility for all patients to express their opposition to the use of data at any time. This report follows the STROBE recommendations (Additional file 1) [25].

Study scheme

This study was a retrospective analysis of a prospectively collected database of patients hospitalized after a hip surgery in a Perioperative Geriatric care Unit (UPOG) of a French tertiary university teaching hospital in Paris (France). The UPOG is part of a dedicated orthogeriatric care pathway, whose main characteristics are: (1) early alert from the emergency department; (2) attempt to perform hip fracture surgery as soon as possible (i.e., day and night); (3) early transfer to the UPOG after surgery; and (4) early rehabilitation starting in the UPOG, and early transfer of stable patients to a dedicated rehabilitation unit [2, 26].

Patient selection

From January 2012 to June 2021, all consecutive patients with hip fracture admitted to the UPOG were screened for eligibility. Patients were included if they were aged 70 years or older and admitted to the UPOG after hip fracture surgery. Patients were excluded if they had periprosthetic, metastatic or multiple fractures, missing data on perioperative use of SSRIs, anticoagulants or antiplatelets drugs, or if they were hospitalized during the liberal transfusion strategy period (before January 1st, 2012) [27]. Patients were followed up from emergency department admission, until death or UPOG discharge.

Data collection

Since the opening of the UPOG in 2009, a dedicated research database has been created and data on all patients have been prospectively collected by 3 senior geriatricians (J.B., J.C-B., S.T.). The database includes patient characteristics such as age, sex, lifestyle, medical history and treatment, SSRI medication, baseline functional capacity and type of fracture. Various scales were calculated by one of the 3 senior geriatricians to assess: functional autonomy with Katz's Activities of Daily Living (ADL) [28] and Instrumental ADL (IADL) scales [29], comorbidity burden with the Charlson Comorbidity Index (CCI) [30], frailty with the Rockwood frailty score [31], and disease severity with the Cumulative Illness Rating Scale (CIRS) [32]. These data refer to the preoperative period and were collected prospectively. On admission at the emergency department, delay before surgery, type of anesthesia, type of surgery, surgery duration, and RBC transfusions were collected. During UPOG stay, occurrence of death, postoperative complications, and length of stay were recorded.

Hemorrhagic events were classified as severe if they required surgical, endoscopic, or radiologic intervention, or if they resulted in clinical instability or death. During the entire hospitalization, SSRI initiation or discontinuation was recorded. Patients with SSRI treatment at admission were included in the "SSRI group", while patients without SSRI treatment at admission were included in the "non-SSRI group". Since we aim to determine whether blood transfusion differs between the two groups, and in order to avoid a difference due to the possible effect of SSRI initiation, patients were included in the SSRI group if SSRI treatment had been discontinued during hospitalization, while patients were included in the non-SSRI group if an SSRI had been initiated during hospitalization.

Endpoints

The primary endpoint was the occurrence of RBC transfusion, evaluated as a binary event (yes/no), during hospitalization, from emergency department admission to UPOG discharge or death. The transfusion strategy was described previously [27]: if acute anemia was associated with hemodynamic instability, acute coronary syndrome or acute heart failure regardless of hemoglobin levels; if hemoglobin was below 8 g/dL for patients with cardiac comorbidities, or below 7 g/dL in all other cases. Secondary endpoints included the number of postoperative packed RBC transfusion (units) per patient, length of hospital stay, in-hospital mortality, and the description of hemorrhagic events that occurred during hospitalization (gastrointestinal bleeding, hematuria, intracerebral hemorrhage, psoas hematoma, mucocutaneous bleeding, and leg hematoma).

Statistical method

A statistical plan discussed between clinicians and statistical analyst was performed prior to the start of the study. Data are expressed as mean ± SD for Gaussian variables, median and 25% to 75% interquartile range for non-Gaussian or discrete variables, and number (with percentages) for categorical variables. Baseline characteristics between groups were compared using the Student *t*-test or Mann–Whitney U test for quantitative variables, and the Chi square test or Fisher's exact test for qualitative variables, as appropriate.

The primary endpoint was analyzed using a logistic regression model. The variables retained for multivariate analysis were age, sex, CCI, functional status, institutionalization, low albumin level, as well as variables known to increase the risk of transfusion, namely: polypharmacy, baseline antiplatelet therapy, intertrochanteric fracture (*versus* cephalic fracture), and hemoglobin level at hospital admission. Stratification by year of enrollment was discussed, and ultimately not performed, as the number of patients on SSRI by year and by type of SSRI did not differ between years of enrollment (Additional files 2 & 3). To test the synergy between SSRI use and antiplatelet therapy on RBC transfusion risk, we a priori planned to calculate an adjusted interaction OR by introducing an interaction term in the logistic regression model between SSRI use and antiplatelet therapy use.

Because serotonin plays a role in primary hemostasis, a subgroup analysis was performed to examine the association between the affinity of the SSRI for serotonin (degree of serotonin reuptake inhibition) and the number of packed RBC per patient transfused postoperatively. Patients were divided into three subgroups: high affinity for serotonin (paroxetine, sertraline, fluoxetine), moderate affinity (escitalopram, citalopram, duloxetine, venlafaxine), and low or no affinity for serotonin (any antidepressant treatment with low effect or without effect on serotonin, or no antidepressant treatment) [16]. This analysis included only patients with at least one postoperative RBC transfusion and described only the median number of packed RBC transfused per patient postoperatively and interquartile range in box plots, without adjustment for confounders.

A first sensitivity analysis was performed to examine the effect of a co-treatment of SSRIs with antiplatelet therapy or anticoagulants on the primary endpoint. Since current use of SSRIs (versus recent discontinuation) has been associated with an increased risk of transfusion in patients undergoing hip fracture surgery [21], and since the effect on hemostasis and bleeding risk is unknown in the days following an initiation of SSRI, a second sensitivity analysis was performed, where the primary endpoint was analyzed after excluding patients with in-hospital initiation of SSRI. These analyses used two logistic regression models adjusted for the same variables used for the primary endpoint. For all tests, the alpha-level was defined as 0.05 bilaterally, and analyses were performed with R Studio 2023.06.0 + 421 version.

Results

Patient characteristics

Out of 1239 patients hospitalized at UPOG from January 2012 to June 2021, 1085 patients were included in the analysis, of whom 245 (20%) were treated with SSRIs (Fig. 1).

The mean age was 86 (± 6.2) years, 253 patients were male (23%), and the median CCI was 7 [5–8]. The median ADL before surgery was 5.5 [3.5–6] and the median IADL was 2 [0–4]; 161 patients (15%) were institutionalized, and 669 (62%) were walking with assistance. The median time to surgery was 27 h [19–48] and 560 (52%) fractures were intertrochanteric. The mean surgery duration was

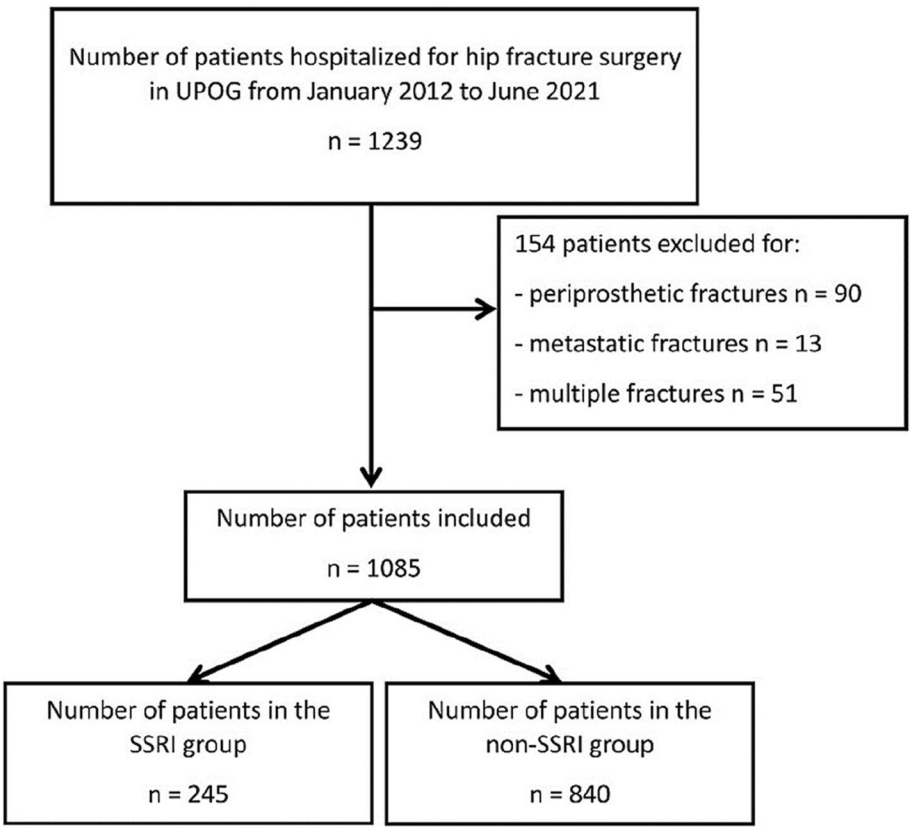

Fig. 1 Flow chart of participants included in the study

134 (±41) minutes and did not differ between patients who received RBC transfusion and those who did not. Baseline characteristics according to the occurrence of transfusion are described in Table 1.

Primary endpoint: blood transfusion

A total of 486 patients (45%) received RBC transfusion, with a median of 2 [1–3] RBC units transfused postoperatively per patient. There was no significant difference in the prevalence of RBC transfusion between the two groups, as shown in Table 2.

Factors associated with RBC transfusion in univariate analysis (OR) and multivariate analysis (aOR) are shown in Table 3. On multivariate analysis, SSRI treatment was not associated with the occurrence of RBC transfusion (aOR 0.91, 95% CI 0.64–1.29, $p=0.59$). Factors significantly associated with RBC transfusion were: age (aOR 1.04 for 1 year increase, 95% CI 1.01–1.06, $p=0.008$), preoperative hemoglobin level (aOR 0.51 for 1 g/dL increase, 95% CI 0.45–0.57, $p<0.001$), polypharmacy (aOR 1.47, 95% CI 1.05–2.06, $p=0.02$), low albumin level (< 30 g/L, aOR = 1.47, 95% CI 1.10–1.97, $p=0.01$), and occurrence of intertrochanteric fracture (aOR 2.11, 95% CI 1.59–2.83, $p<0.001$). Additional file 4 shows the results of the multivariate analysis of factors associated with RBC transfusion when adding the year of fracture in the model. There was no synergistic effect of concomitant use of antiplatelets and SSRIs on the risk of RBC transfusion: OR 1.47 (95% CI 0.72–3.03, $p=0.30$).

Other endpoints

Table 2 shows the occurrence of other outcomes in patients treated with or without SSRIs. Hemorrhagic events occurred in 19 patients in the SSRI group (7.8%) and in 76 (9%) patients in the non-SSRI group ($p=0.16$). The most common hemorrhagic events were leg hematoma and gastrointestinal bleeding. The in-hospital mortality rate was 34 (3.1%) in the entire cohort, with 9 (3.7%) deaths in the SSRI group and 25 (3%) deaths among the non-SSRI group ($p=0.54$). The median hospital length of stay was 9 days [7–12] and did not differ between the two groups.

Subgroup and sensitivity analysis

The subgroup analysis of the number of postoperative RBC transfusion according to the affinity of SSRIs for serotonin are shown in Additional file 5. The median number of RBC transfusion was 2 [1, 2] units per patient

Table 1 Baseline characteristics

	All ***N*** **= 1085**	**Not transfused** ***N*** **= 599**	**Transfused** ***N*** **= 486**	***P*** **value**
Age (years)	86 (± 6.2)	85.6 (± 6.2)	87.4 (± 6.5)	< 0.001
< 85	375 (35)	231 (39)	144 (30)	0.002
85 to 90	414 (38)	236 (39)	178 (37)	0.35
> 90	296 (27)	132 (22)	164 (34)	< 0.001
Male	253 (23)	141 (24)	112 (23)	0.85
Weight (kg)	58.7 (± 13.2)	60.0 (± 13.4)	57.2 (± 12.5)	< 0.001
Autonomy before surgery				
ADL	5.5 [3.5–6]	5.5 [4–6]	5 [3.5–6]	0.002
IADL	2 [0–4]	2 [0–4]	2 [0–3]	0.02
Living in institution	161 (15)	84 (14)	77 (16)	0.40
Walking with assistance	669 (62)	341 (57)	328 (68)	< 0.001
Medical history				
CIRS	9 [7–12]	8 [6–12]	10 [8–14]	< 0.001
Charlson Comorbidity Index	7 [5–8]	6 [4–8]	7 [5–9]	< 0.001
Atrial fibrillation	307 (28)	156 (26)	151 (31)	0.07
Coronary artery disease	206 (19)	79 (13)	127 (26)	< 0.001
Cardiac failure	180 (17)	70 (12)	110 (23)	< 0.001
Depression	399 (37)	190 (32)	149 (31)	0.71
Treatments				
Oral anticoagulant	226 (21)	124 (21)	102 (21)	0.91
Antiplatelet	378 (35)	176 (29)	202 (42)	< 0.001
Proton pomp inhibitors	358 (33)	168 (28)	190 (39)	< 0.001
NSAIDs	8 (0.7)	5 (0.8)	3 (0.6)	0.48
Polypharmacy[a]	687 (63)	338 (56)	349 (72)	< 0.001
Fracture				
Intertrochanteric fracture	560 (52)	245 (41)	315 (65)	< 0.001
Femoral neck fracture	522 (48)	354 (59)	168 (35)	< 0.001
Surgery				
Time to surgery (h)	27 [19–48]	28 [20–48]	26 [19–46]	0.04
Gamma nail	559 (52)	243 (41)	313 (64)	< 0.001
Dynamic hip screw	36 (3.3)	30 (5)	6 (1.2)	< 0.001
Unipolar prosthesis	451 (42)	302 (50)	149 (31)	< 0.001
Bipolar prosthesis	20 (1.8)	9 (1.5)	11 (2.3)	0.35
Preoperative biology				
Preoperative Hemoglobin (g/dl)	12.2 (± 1.7)	12.9 (± 1.6)	11.4 (± 1.8)	< 0.001
Creatinine at admission (µmol/l)	74.5 (± 39.1)	71.4 (± 30.1)	78.2 (± 47.8)	0.004
Missing values	*1 (0.1)*	*0 (0)*	*1(0.2)*	-
Albumine (g/l)	29.0 (± 4.0)	29.7 (± 4.1)	28.1 (± 3.7)	< 0.001

Data are mean (± SD), median (25–75 interquartile range), or number (percentage). Comparison between the two groups by t test or Mann–Whitney U test for quantitative variables and chi-square test or Fisher's exact test for qualitative variables. Missing values are specified only if they were present

Abbreviations: *CIRS* cumulative illness rating scale, *ADL* activities of daily living, *IADL* instrumental activities of Daily Living, *NSAIDs* non-steroidal anti-inflammatory drugs

[a] Number of medications > 4

in the groups with moderate ($p = 0.32$) and high affinity ($p = 0.42$) for serotonin, and 2 [1–3] units per patient in patients without antidepressants or with antidepressants with low affinity or without affinity for serotonin (reference group).

A first sensitivity analysis did not find any association between the occurrence of RBC transfusion and the concomitant use of SSRIs and treatments modifying hemostasis, as shown in Additional file 6 (aOR 0.75, 95% CI 0.36–1.57 for patients on both SSRIs and anticoagulants,

Table 2 Blood transfusion and hemorrhagic events during hospitalization

	All *N* = 1085	Non-SSRI group *N* = 840	SSRI group *N* = 245	*P* value
Blood transfusion				
Occurrence during hospital stay	486 (45)	377 (45)	109 (45)	0.91
RBC transfused postoperatively (units per patient)[a]	2 [1–3]	2 [1–3]	2 [1, 2]	0.56
Hemorrhagic events				
All types	95 (8.8)	76 (9)	19 (7.8)	0.16
Severe	30 (2.8)	26 (3.1)	4 (1.6)	0.22
Hematuria	3 (0.3)	1 (0.1)	2 (0.8)	0.08
Digestive bleeding	15 (1.4)	13 (1.5)	2 (0.8)	0.99
Psoas Hematoma	2 (0.2)	1 (0.1)	1 (0.4)	0.32
Leg Hematoma	60 (5.5)	50 (6)	10 (4.1)	0.76
Intracerebral bleeding	1 (0.1)	1 (0.1)	0 (0)	0.99
Mucocutaneous bleeding	3 (0.3)	3 (0.4)	0 (0)	0.99
Missing values	*11 (1)*	*7 (0.8)*	*4 (1.6)*	-
Other outcomes				
Intra-hospital death	34 (3.1)	25 (3)	9 (3.7)	0.54
LOS (days)	9 [7–12]	9 [7–12]	9 [7–12]	0.50

Data are mean ± SD or number (percentage). Comparison between the two groups by t test or Mann–Whitney U test for quantitative variables and chi-square test or Fisher's exact test for qualitative variables. Missing values are specified only if they were present

Abbreviations: LOS Length of stay (in days), *RBC* Red Blood Cells packs

[a] Among those receiving postoperative RBC transfusion

Table 3 Univariate and multivariate analysis of factors associated with RBC transfusion

	OR	$CI_{95\%}$	aOR[a]	$CI_{95\%}$	p_{value}
Baseline					
Age (for 1 year increase)	1.05	1.03–1.07	1.04	1.01–1.06	0.008
Sex (Male)	0.97	0.72–1.30	1.13	0.79–1.61	0.50
CCI (for 1 point increase)	1.14	1.08–1.19	1.02	0.96–1.10	0.51
Walking with assistance	1.57	1.21–2.03	1.01	0.74–1.39	0.95
Living in institution	1.15	0.81–1.64	0.89	0.59–1.34	0.58
Albumin < 30 g/l	1.87	1.44–2.42	1.47	1.10–1.97	0.01
Preoperative hemoglobin (for 1 g/dl increase)	0.47	0.42–0.53	0.51	0.45–0.57	< 0.001
Treatments					
SSRI	0.98	0.73–1.32	0.91	0.64–1.29	0.59
Antiplatelets therapy	1.71	1.32–2.22	1.35	0.98–1.85	0.07
Polypharmacy[b]	1.97	1.51–2.56	1.47	1.05–2.06	0.02
Surgery					
Intertrochanteric fracture	2.66	2.06–3.44	2.11	1.59–2.83	< 0.001

N = 1048, AIC = 1150.4

Abbreviations: *CCI* Charlson Comorbidity Index, *RBC* Red Blood Cells, *SSRI* Selective Serotonin reuptake inhibitors

[a] aOR: multivariate analysis adjusted for age, sex, CCI, walking with assistance, living in institution, albumin level, preoperative hemoglobin, antiplatelets therapy, polypharmacy, and intertrochanteric fracture

[b] Number of medication > 4

and aOR 1.20, 95% CI 0.67–2.18 in patients on both SSRIs and antiplatelets therapy). A second sensitivity analysis excluding patients to whom an SSRI was initiated during hospital stay found no significant association between SSRI use and the occurrence of RBC transfusion (aOR 0.92, 95% CI 0.65–1.31).

Discussion

In this retrospective analysis of a large prospective database of older adults undergoing hip fracture surgery, we aimed to investigate whether the use of SSRIs is associated with the risk of perioperative RBC transfusion in adults aged 70 years and older. After adjustment for age, sex, comorbidities, functional ability, institutionalization, low baseline albumin level, antiplatelet agent therapy, polypharmacy, type of hip fracture, and preoperative hemoglobin, the use of SSRIs was not associated with an increased incidence of RBC transfusion.

In our study, forty-five percent of patients received perioperative RBC transfusion. This result is consistent with those reported in previous cohorts of patients undergoing hip fracture surgery, in which 30% to 58% of patients received RBC transfusions [5, 6, 23, 33]. The high prevalence of RBC transfusion in our cohort could be explained by an older age, the low use of dynamic hip screws, and the high prevalence of polypharmacy, antiplatelet therapy and anticoagulants. In addition, the

risk factors for RBC transfusion were similar to those reported in previous studies, as age, preoperative hemoglobin, and intertrochanteric fracture [6]. As in the Danish study, the risk of perioperative bleeding did not differ between SSRI users and non-users [34].

The impact of SSRI use on RBC transfusion has not been studied in the older comorbid population with polypharmacy. In the study of Schutte et al. [23], patients undergoing hip fracture surgery were younger with a mean age of 77 years and had less comorbidities. In addition, patients on SSRI treatment were underrepresented in the cohort, and polypharmacy was not described. In a second study including patients from an orthopedic surgery ward, the mean age was 68 years, with only 69% of the cohort undergoing hip fracture surgery [22]. Again, SSRI use was underrepresented in the cohort (5%) and the prevalence of comorbidities was low. In the Danish study, the mean age was closer to our cohort (85 years), but the study focused on the association between SSRI use and bleeding risk, and not RBC transfusion [34]. We chose to use RBC transfusion as primary outcome in order to avoid bias due to potential missing data.

Our study is the first to evaluate the impact of SSRI use on the risk of RBC transfusion in highly comorbid patients with polypharmacy, undergoing hip fracture surgery. Given that patients with cardiovascular diseases have a higher transfusion threshold [35], the high prevalence of heart failure and coronary artery disease could potentially impact our findings. Previous studies have reported heart failure rates ranging from 3 to 9% [22, 34]. None of them describe polypharmacy, despite its known association with increased bleeding risk [36]. Our results indicate a higher frequency of proton pump inhibitors use among patients who received RBC transfusion, suggesting a possible history of gastrointestinal bleeding. Additionally, our study is the only one to analyze the risk of transfusion in patients taking SSRIs according to the molecule's affinity for serotonin. Thus, our cohort is highly representative of the older comorbid population commonly admitted to geriatric wards and undergoing hip fracture surgery.

Previous studies have shown an increased risk of bleeding events in the perioperative setting [37–39]. Therefore, the benefit/risk balance of stopping SSRIs has been questioned. Indeed, Jeong et al. recommend stopping SSRIs preoperatively in scheduled surgeries to limit bleeding risk [24]. However, stopping antidepressants could have as a consequence to induce delirium, withdrawal syndrome or relapse of depression [40–43]. In the context of acute surgery in a highly comorbid population, these complications could negatively influence the outcome in geriatric patients [3]. Stopping SSRIs prior to hip fracture surgery could have as a consequence an increase in delay before surgery, negatively influencing patient outcome, as an increased delay before hip fracture surgery is associated with an increased 30-day mortality [44]. Thus, after adjusting for age, comorbidities, functional status, polypharmacy, surgical characteristics, hemoglobin and albumin levels, our findings suggest that patients receiving SSRIs could undergo surgery without delay. Our results suggest that physicians should not discontinue SSRIs during the perioperative stay, especially in an aged and comorbid population. On the other hand, physicians should concentrate their efforts on applying Patient Blood Management principles, such as managing medication and interactions, controlling hemostatic disorders, optimizing cardiopulmonary function, adapting surgical techniques in order to limit RBC transfusion, improve patient outcome and decrease hospitalization duration [45].

Our study has several limitations to be acknowledged. First, the data collection was performed prospectively, but the analysis was performed retrospectively, with a database that was not specifically designed for this analysis. Additionally, the study was monocentric and observational. Further studies are needed to confirm our results. Secondly, to limit bias caused by potentially missing data on hemorrhagic events, RBC transfusion was used as a surrogate marker for severe bleeding complications. However, it is important to note that some severe bleeding complications, such as intracerebral hemorrhage and hematuria, may not always require RBC transfusion. These complications were infrequent, with intracerebral hemorrhage occurring in only one patient, and hematuria in three patients. Third, we do not have the date of SSRI initiation in relation to the occurrence of the bleeding event in patients to whom SSRI was introduced during hospitalization. However, among 23 patients in whom SSRI was introduced during hospitalization, only one bleeding event was reported. This event was a stomach hemorrhage in a cancer patient receiving anticoagulant therapy for atrial fibrillation. In addition, the sensitivity analysis which excluded patients with SSRI initiation during hospitalization yielded similar results.

Our study has several strengths: inclusion of a large sample size, with patients that are representative of a population seen in geriatric units, in terms of age, comorbidities, loss of functional ability, and polypharmacy. A robust and clinically relevant outcome of RBC transfusion was used as primary endpoint. There was no missing data regarding concomitant use of antiplatelet agents/anticoagulants and RBC transfusion. To avoid a possible difference related to SSRI introduction effect, patients who were initiated to SSRIs during hospitalization were included in the non-users group. Our results are

supported by the sensitivity analysis, which allowed us to study co-prescriptions in detail.

Conclusions

In conclusion, this is the first study evaluating the risk of perioperative RBC transfusion on SSRI treatment in a large, older, and comorbid population of patients hospitalized in a geriatric ward for hip fracture surgery. After adjusting for baseline characteristics, functional ability, co-treatments, surgical characteristics, baseline hemoglobin and albumin, the use of SSRIs was not found to be associated with an increased risk of RBC transfusion. In this setting, our findings add additional insights in the benefit/risk balance of discontinuing SSRIs prior to hip fracture surgery.

Abbreviations

ADL	Activities of daily living
AP-HP	Public assistance of Paris hospitals
CCI	Charlson comorbidity index
CIRS	Cumulative illness rating scale
CNIL	French National Commission on Computing and Liberty
IADL	Instrumental activities of daily living
NSAIDs	Non-steroidal anti-inflammatory drugs
RBC	Red blood cell
SSRI	Selective serotonin reuptake inhibitors
UPOG	Perioperative Geriatric care Unit

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12877-024-05634-6.

Additional file 1. STROBE Statement. Table with the STROBE checklist.

Additional file 2. Annual antidepressant prescription profile in UPOG between 2012 and 2021. Histograms of the number of patients taking antidepressants by drugs and years.

Additional file 3. Annual antidepressant prescription profile in UPOG between 2012 and 2021. Table of the number of patients taking antidepressants by drugs and years.

Additional file 4. Multivariate analysis of factors associated with RBC transfusion, with the year of fracture added to the model.

Additional file 5. Subgroup analysis of number of RBC transfused postoperatively regarding to serotonin affinity. Boxplots of the subgroup analysis.

Additional file 6. Multivariate analysis of the association of SSRI use with the occurrence of RBC transfusion among patients with or without antiplatelet or anticoagulant therapy.

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Authors' contributions

ST, JB, LZ, BG and HG-M contributed to conception, design of the study and acquisition of data. Judith Cohen-Bittan contributed to acquisition of data. ST, LZ, BG and HG-M contributed to analysis and interpretation of data. MR contributed to interpretation of data. HG-M completed the first draft of the manuscript with the supervision of ST, and the remaining authors contributed to critical revision of the final manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets analyzed during the current study are available from author Pr Jacques Boddaert on reasonable request (jacques.boddaert@aphp.fr), on the condition that the research project is accepted by the Ile de France VI's Scientific and Ethics Committee.

Declarations

Ethics approval and consent to participate

All methods were performed in accordance with the relevant guidelines and regulations (https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037187498). The study was approved by the Ile de France VI's Scientific and Ethics Committee, Paris, France; and the database was declared to the French National Commission on Computing and Liberty (CNIL) of AP-HP (registration n°20190426181554). The need for informed consent was waived by the Ile de France VI's Scientific and Ethics Committee, because of the retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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