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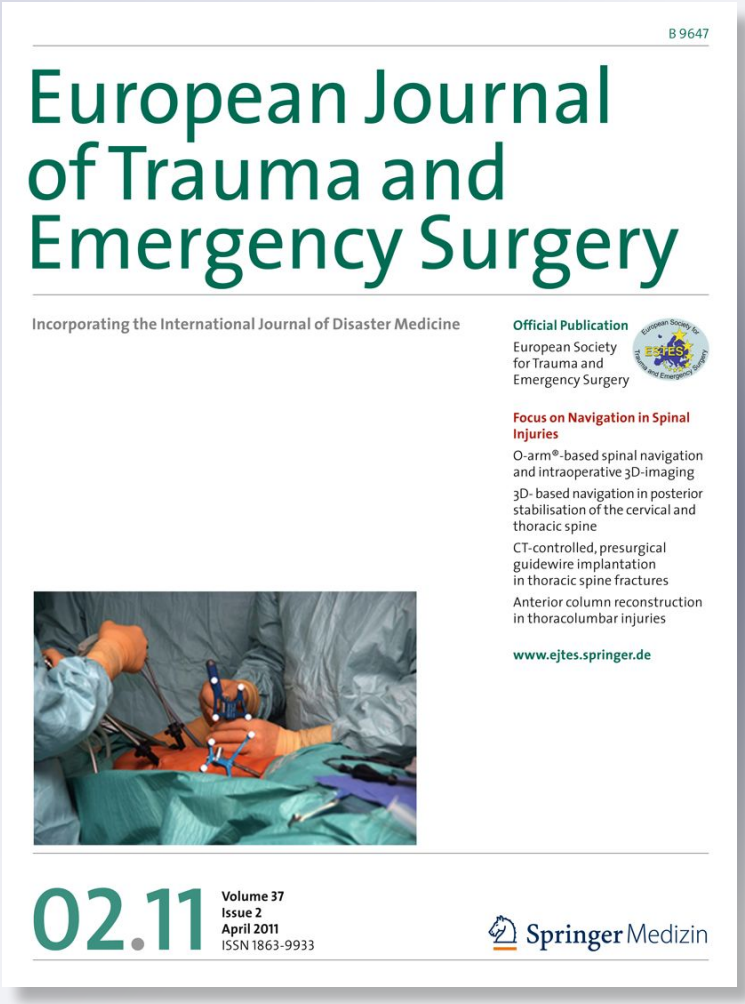


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ORIGINAL ARTICLE

# Influence of timing and oral anticoagulant/antiplatelet therapy on outcomes of patients affected by hip fractures

**F. Dettoni · F. Castoldi · A. Giai Via · S. Parisi · D. E. Bonasia · R. Rossi**

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**Abstract**
*Background* Patients undergoing surgical procedures are usually asked to discontinue any anticoagulant/antiplatelet therapy and delay surgery for at least 5 days to reduce the risk of major bleeding and spinal hematoma.
*Aim* The purpose of this study was to determine if this strategy is suitable for patients on anticoagulant/antiplatelet therapy affected by a hip fracture, evaluating the effect of anticoagulant/antiplatelet therapy and surgical timing on mortality and complication rates for patients affected by a hip fracture.
*Patients and methods* We performed an observational study on patients referring to our hospital for a hip fracture. We evaluated patients on warfarin, ticlopidine, and aspirin therapy matched to patients not on anticoagulant or antiplatelet therapy, out of 875 consecutive patients treated for a hip fracture in a 5-year period. Blood loss, blood transfusions, length of hospitalization, walking ability, complications, and mortality at 1 year of follow-up were recorded. Kruskal–Wallis, Mann–Whitney *U*, and logistic regression statistical tests were performed.
*Results* Patients on warfarin therapy operated more than 5 days after admission showed significantly higher complication and mortality rates compared to all other patients. Two critical factors were identified: warfarin therapy and excessive time to surgery; these factors are not significant if taken alone, while they become a high-risk factor if taken together.
*Conclusion* The "discontinue drug, and delay surgery" strategy is not suitable for patients on anticoagulant (warfarin) therapy affected by a hip fracture.

**Keywords** Hip fracture · Anticoagulant therapy · Antiaggregant therapy · Mortality · Complications · Warfarin

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## Introduction

"Time to surgery" (waiting time between admission and surgery) for hip fracture (HF) patients is a long debated argument. For the elderly patients, it is often necessary to delay surgery in order to restore general conditions to clinical stability; nonetheless, many investigators found an increasing mortality directly connected to a longer waiting time [1–5]. One of the reasons for the delay is that some patients are under anticoagulant or antiplatelet therapy, and a washout period is required in order to perform surgery under safer conditions. In the last several decades, patients who assume oral anticoagulant therapy have been increasing and warfarin has become commonly used, especially in patients affected by atrial fibrillation, deep vein thrombosis (DVT), or valve replacement [6–8]. It has been estimated that nearly 1.5% of the population is on warfarin therapy for cardiovascular disease prophylaxis [9–11]. The use of antiplatelet (antiaggregant) therapies such as aspirin and ticlopidine has increased also in the last few years, for example, in the secondary prevention for myocardial infarction or neurovascular diseases [12].

The major risks for early surgery in patients on antiaggregant therapy (AAT) are blood loss and spinal hematoma

(when peripheral anesthesia is performed) [13–17]. In order to avoid these risks, therapy is discontinued (and usually substituted by low-molecular-weight heparin) and the surgical treatment is postponed until the International Normalized Ratio of prothrombin time (PT-INR) returns to the normal range (usually 0.8–1.2). Many papers in the literature and medical societies suggest, therefore, for patients on AAT undergoing a surgical procedure to discontinue therapy and delay surgery for at least 5 days in order to allow drug washout [18–20]. But while this strategy is applicable to elective surgery with relatively no contraindication, in patients affected by HF, a delay of surgery of 5 or more days is questionable; in fact, while the effect of AAT on blood loss and risk of spinal hematoma is still debated, it is proved beyond doubt that a delay in surgery increases the rate of major complications and mortality [21].

The aim of this study was to evaluate the incidence of complications related to "time to surgery" and AAT in patients affected by HF and to determine whether a "discontinue drug, and delay surgery" strategy is advised, or if, in this population of patients, another strategy should be considered.

We analyzed the outcomes, in terms of mortality, complications, blood loss, and functional recovery, obtained by patients.

## Patients and methods

We matched five groups of patients out of 875 consecutive patients treated in our orthopedic division for HF (both cervical and trochanteric fractures of the proximal femur) in a 5-year period. Each group was composed of 30 patients: group A included patients on warfarin therapy, who had to wait 5 or more days before surgery (in order to obtain drug washout); group B included patients on ticlopidine therapy that waited more than 5 days for surgery; group C included patients on aspirin therapy that waited more than 5 days for surgery; group D included patients not on anticoagulant nor antiplatelet therapy, but with the same time to surgery (>5 days); and group E included patients who were not on AAT, operated within 48 h from admission.

The inclusion criteria were: age over 65 years, no high-energy trauma (e.g., motor vehicle accident), operative treatment (non-operative treatments were excluded), AAT for cardiac arrhythmia (i.e., atrial fibrillation), AAT for no more than 5 years, American Society of Anesthesiologists (ASA) score <3, no major neurological/cognitive deficiency, no hematological disease (i.e., coagulopathy, immunohematological disorders), no rheumatologic disorders, no chronic hepatopathies, no cardiovascular disease such as cardiac ischemia and cerebral vasculopathy, no metastatic neoplasia, INR <4 at admission, no immunosuppressor therapy.

The number of patients in each group was determined by the smallest group: out of the 875 patients, 49 were on warfarin therapy and 30 matched the inclusion criteria. Patients in the other four groups were selected from a pool of patients eligible (according to the inclusion criteria), choosing the patients that matched more closely to the 30 patients in the warfarin group (on the basis of gender, age, fracture pattern, and surgical treatment).

With these inclusion criteria and matching method, the five groups were comparable regarding gender, mean age, fracture pattern, and surgical treatment (intramedullary nailing vs. hemiarthroplasty). (Table 1).

Surgery was performed by the same staff, according to the same surgical techniques, using the same implants: Gamma 3 (Stryker Trauma GmbH, Schoenkirchen, Germany) intramedullary nailing in trochanteric fractures and Ellittica (Samo, Bologna, Italy) cemented hemiarthroplasty via a posterolateral approach in cervical fractures.

All patients underwent a similar postoperative protocol, consisting of early mobilization on the first postoperative day, with weight-bearing as tolerated on the injured limb, and rehabilitation in the outpatient clinic or in a rehabilitation facility for 3–6 weeks according to the patient's needs.

We recorded the preoperative blood loss, number of red blood cell (RBC) units transfused (before and after surgery), length of hospitalization (time to surgery + time from surgery to discharge), walking ability reached after surgery, major complications arising during hospitalization and up to 12 months after surgery (DVT, EP, urinary, respiratory, and surgical site infections, and cardiovascular diseases such as stroke and MI), and survivorship at 1 year of follow-up.

Data were acquired via hospital charts investigation and a questionnaire performed at least 12 months after hospital discharge, driven by one of the authors (SP) questioning the patients directly in the outpatient clinic or over the phone (if the patient refused or was unable to reach our

**Table 1** Groups of patients used in this study

| Group | Number of patients | Gender | Treatment | Age, mean (SD) |
|---|---|---|---|---|
| Group A | 30 | 6 M/24 F | 15 IN/15 HA | 83.3 (7.6) |
| Group B | 30 | 6 M/24 F | 15 IN/15 HA | 84.5 (6.3) |
| Group C | 30 | 5 M/15 F | 15 IN/15 HA | 81.5 (7.9) |
| Group D | 30 | 6 M/24 F | 15 IN/15 HA | 84.7 (6.2) |
| Group E | 30 | 5 M/15 F | 15 IN/15 HA | 85.5 (5.4) |

*M* male; *F* female; *IN* intramedullary nail; *HA* hemiarthroplasty; *SD* standard deviation

hospital); if the patients were unable to sustain a phone call (due to any kind of impairment, poor compliance, or death of the patient), a relative was questioned.

Walking ability was subjectively defined by the patient as the percentage of recovery in comparison to prefracture ability.

Two patients that were selected for this study were unavailable for the phone call, so they were substituted for our study purposes by two other patients belonging to the same cohort of 875 HF patients.

### Ethics

All patients gave an informed consent to be included in the study. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki as revised in 2000. No ethical committee was questioned, since this observational study could be of no harm for the patients.

### Statistical analysis

Data were collected and stored in a database on a personal computer via an MS Office Excel$^{TM}$ spreadsheet file. Statistical analysis was performed using the Kruskal–Wallis, Mann–Whitney *U*, and logistic regression tests.

Kruskal–Wallis is a non-parametric method for testing the equality of population medians among groups [22]. The Mann–Whitney *U*-test (also called the Mann–Whitney–Wilcoxon, Wilcoxon rank-sum test, or Wilcoxon–Mann–Whitney test) is a non-parametric test for assessing whether two samples of observations come from the same distribution. It is one of the best-known non-parametric significance tests [23]. Logistic regression provides a method for modeling a binary response variable [24]. The Statistical Package for the Social Sciences (SPSS) 16.0, Stata (Statistical Da-ta) 3.0, and Minitab 14.0 software packages were used to analyze the data, under the supervision of an expert statistician.

The power of this study was determined post-hoc, using G*Power 3.0.10 software.

The effect size $f$ and statistical power $(1 - \beta)$ are reported at the end of the results section. The effect of the size of the samples and of the differences in patients' health status in the five different groups was not clearly predictable, but it could be argued that patients in group B and particularly in group A had a worse health status and, therefore, worse results should be expected. The inclusion and exclusion criteria were designed for the purpose of reducing this risk, excluding from our study the patients with a worse general health status.

## Results

Tables 2, 3, and 4 report the blood loss of the different groups, expressed in hemoglobin levels, and the number of blood transfusions performed. Hemoglobin levels were determined at admission and within 6 h before (preoperative) and 6 h after (postoperative) operation.

**Table 2** Hemoglobin levels at admission and before operation (within 6 h from operation)

| Group | Admission hemoglobin (mg/dL) | Preoperative hemoglobin (mg/dL) | Preoperative hemoglobin loss (mg/dL) | *p*-value K–W | *p*-value M–W |
|---|---|---|---|---|---|
| Group A | 13.1 (SD 1.2) | 11.7 (SD 1.2) | 1.4 (SD 1) | >0.05 | 0.037 |
| Group B | 12.7 (SD 1.4) | 11.8 (SD 1.4) | 0.9 (SD 0.9) | | 0.028 |
| Group C | 12.4 (SD 1.6) | 11.9 (SD 1.5) | 0.5 (SD 1.1) | | 0.000 |
| Group D | 12.9 (SD 1.5) | 12.0 (SD 1.6) | 0.9 (SD 1.2) | | 0.025 |
| Group E | 12.3 (SD 1.9) | 11.7 (SD 1.7) | 0.6 (SD 1.1) | | 0.017 |

*SD* standard deviation; *K–W* Kruskal–Wallis between groups; *M–W* Mann–Whitney: specific subgroup versus all other groups

**Table 3** Mean hemoglobin levels before and after operation (within 6 h before and after operation)

| | Preoperative hemoglobin (mg/dL) | Postoperative hemoglobin (mg/dL) | Intra-operative blood loss (mg/dL) | *p*-value K–W | *p*-value M–W |
|---|---|---|---|---|---|
| Group A | 11.7 (SD 1.16) | 10.3 (SD 1.2) | 1.1 (SD 1.3) | >0.05 | 0.042 |
| Group B | 12.0 (SD 1.6) | 11.2 (SD 1.6) | 0.8 (SD 1.0) | | 0.032 |
| Group C | 11.7 (SD 1.7) | 10.8 (SD 1.7) | 0.8 (SD 0.8) | | 0.042 |
| Group D | 11.8 (SD 1.4) | 11.0 (SD 1.4) | 0.9 (SD 1.1) | | 0.045 |
| Group E | 11.9 (SD 1.5) | 10.6 (SD 1.5) | 1.3 (SD 1.3) | | 0. 071 |

*SD* standard deviation; *K–W* Kruskal–Wallis between groups; *M–W* Mann–Whitney: specific subgroup versus all other groups

**Table 4** Mean number of blood unit transfusions during hospital stay

| | Number of transfusions | Number of transfusions (IN) | Number of transfusions (HA) | *p*-value K–W | *p*-value M–W |
|---|---|---|---|---|---|
| Group A | 1.5 (SD 1.9) | 1.7 (SD 1.9) | 1.3 (SD 1.9) | n.s. | 0.122 |
| Group B | 1.6 (SD 1.5) | 1.5 (SD 1.2) | 1.7 (SD 1.8) | | |
| Group C | 1.6 (SD 1.3) | 2.4 (SD 1.3) | 0.9 (SD 0.8) | | 0.327 |
| Group D | 1.2 (SD 1.4) | 1.7 (SD 1.6) | 0.6 (SD 0.8) | | 0.043 |
| Group E | 1.5 (SD 1.6) | 1.8 (SD 1.7) | 1.2 (SD 1.6) | | 0.077 |
| Total | 1.6 (SD 1.4) | 1.7 (SD 1.6) | 1.1 (SD 1.4) | | 0.005 |

*SD* standard deviation; *IN* intramedullary nail; *HA* hemiarthroplasty; *K–W* Kruskal–Wallis between groups; *M–W* Mann–Whitney: specific subgroup versus all other groups; *n.s.* not significant

**Table 5** Length of hospitalization

| | Length of hospitalization | Length of hospitalization (IN) | Length of hospitalization (HA) | *p*-value K–W | *p*-value M–W |
|---|---|---|---|---|---|
| Group A | 17.9 (SD 5.9) | 16.3 (SD 5.3) | 19.4 (SD 6.3) | <0.001 | Group A vs. E: 0.000 |
| Group B | 16.3 (SD 6.6) | 16.1 (SD 6.8) | 16.5 (SD 6.6) | | Group B vs. E: 0.005 |
| Group C | 15.4 (SD 6.4) | 17.6 (SD 7.3) | 13.3 (SD 4.6) | | Group C vs. E: 0.026 |
| Group D | 17.4 (SD 5.5) | 16.7 (SD 4.7) | 18.1 (SD 6.3) | | Group D vs. E: 0.000 |
| Group E | 11.8 (SD 4.1) | 11.2 (SD 3.2) | 12.4 (SD 4.9) | | All other comparisons between groups: n.s. |
| Total | 15.7 (SD 5.9) | 15.6 (SD 5.9) | 15.9 (SD 6.3) | | |

*SD* standard deviation; *IN* intramedullary nail; *HA* hemiarthroplasty; *K–W* Kruskal–Wallis between groups; *M–W* Mann–Whitney; *n.s.* not significant

**Table 6** Recovery of walking ability: walking ability restored, expressed as the percentage of prefracture walking ability

| | Walking ability | *p*-value K–W |
|---|---|---|
| Group A | 48 (IN: 50, HA: 45) | n.s. for anticoagulant therapy |
| Group B | 58 (IN: 58, HA: 57) | |
| Group C | 56 (IN: 49, HA: 63) | n.s. for surgical treatment |
| Group D | 60 (IN: 45, HA: 76) | |
| Group E | 59 (IN: 71, HA: 49) | |

*IN* intramedullary nail; *HA* hemiarthroplasty; *K–W* Kruskal–Wallis between groups; *n.s.* not significant

**Table 7** Number of patients affected by major postoperative complications

| | Complications | No complication | *p*-value M–W |
|---|---|---|---|
| Group A | 18 | 12 | A–E: 0.009 |
| Group B | 6 | 24 | All other comparisons between groups: n.s. |
| Group C | 7 | 23 | |
| Group D | 11 | 19 | |
| Group E | 8 | 22 | |

*M–W* Mann–Whitney; *n.s.* not significant

Group A (patients on warfarin therapy) had a higher preoperative blood loss compared to all other groups: mean 1.4 mg/dl hemoglobin (SD = 0.9, $p = 0.002$), but the number of RBC transfusions did not differ from the other groups (Table 3).

We found that the variable which significantly influenced the number of RBC transfusions was the surgical treatment adopted: patients treated with intramedullary nailing needed more transfusions (mean 1.7 RBC units, SD 1.6) than hemiarthroplasties (mean 1.1 RBC units, SD 1.4).

Group A had a longer hospitalization compared to all other groups (except group D): the mean overall hospitalization was 17.9 days (SD = 5.9 $p < 0.001$). The surgical treatment did not influence the duration of hospitalization (Table 5).

We did not find any significant difference regarding walking ability achieved after surgery in correlation to neither AAT (no difference between groups) nor to any other variable considered. Nevertheless, surgical treatment appears to influence walking recovery: postoperative complications affect the walking ability of patients treated by intramedullary nailing more than hemiarthroplasty patients (Table 6).

Patients in group A showed a significantly higher complication rate compared to all other groups; interestingly, the difference is not significant if timing and warfarin therapy are considered as a standalone risk factor, while the difference becomes statistically significant if the two factors are taken together ($p = 0.009$) (Mann–Whitney analysis) (Table 7).

Group A showed a significantly higher mortality at 6 months and at 1 year than groups C, D, and E. Group B

**Table 8** Odds ratio for mortality at 1 year of follow-up

| | Odds ratio | *z*-test | *p*-value | 95% confidence interval |
|---|---|---|---|---|
| Group A | 3.63 | 1.92 | 0.055 | 0.97–13.53 |
| Group B | 1.89 | 0.94 | 0.347 | 0.50–7.12 |
| Group C | 1.44 | 0.53 | 0.596 | 0.37–5.51 |
| Group D | 0.65 | −0.6 | 0.546 | 0.16–2.64 |
| Surgical treatment: IN vs. HA | 1.81 | 1.39 | 0.165 | 0.78–4.18 |
| Gender: F vs. M | 0.94 | −0.11 | 0.911 | 0.30–2.92 |

*IN* intramedullary nail; *HA* hemiarthroplasty; *F* female; *M* male

showed lower 6 months and 1 year mortality compared to group A, but higher 6 months and 1 year mortality compared to groups C, D, and E; however, the differences were not significant. The odds ratio (OR) for patients on warfarin is 3.63 (95% confidence interval [CI] = 0.97–13.53; $p = 0.055$) and it is independent from gender and surgical treatment, but directly proportional to age, while the OR for patients on ticlopidine is 1.89 (95% CI = 0.50–7.12; $p = 0.347$) and the OR for patients on aspirin is 1.44 (95% CI = 0.37–5.51; $p = 0.596$) (Table 8).

Given an $\alpha = 0.05$, the calculated effect size $f$ for mortality was 0.325 and the statistical power $(1 - \beta)$ was 0.900. For blood loss, the effect size $f$ was 0.190 and the statistical power $(1 - \beta)$ was 0.416. For the rate of complications, the effect size $f$ was 0.289 and the statistical power $(1 - \beta)$ was 0.807. For functional recovery, the effect size $f$ was 0.215 and the statistical power $(1 - \beta)$ was 0.522.

## Discussion

The literature shows that patients affected by HF are at high risk of mortality or severe complications [25]. In order to determine the main factors associated to mortality and complications, studies have been conducted, but with controversial results [26].

However, there is a general agreement in considering the increase in pre-, intra-, and postoperative blood loss in patients under AAT requiring surgery to be an important risk factor [6, 9, 19, 27, 28]. Many authors suggest that the INR of these patients at the time of surgery should be at least below 2 [29].

Another important feature to evaluate in patients on AAT is correlated to the anesthesiologic technique used; in peripheral anesthesias it has been reported an increased risk of spinal hematoma. The risk ratio in healthy patients is 1:220,000 with spinal anesthesia and 1:150,000 with neuraxial anesthesia [12]. Risk increases in female patients up to 1:3,600. Spinal hematoma in patients on AAT is very rare, but surely life-threatening [8, 12, 30]. In the literature, it has been reported only two cases of spinal hematoma occurring in patients under warfarin therapy who underwent orthopedic surgery [12, 31, 32], and one case in a non-orthopedic patient under ticlopidine therapy [33]. There is no evidence in the literature as to whether aspirin determines a higher risk of blood loss, nor if it raises the risk of spinal hematoma [34], nor any case of spinal hematoma attributable to aspirin therapy has ever been reported.

Many studies have shown a wide safety margin using low-molecular-weight-heparin, either in spinal or neuraxial anesthesia [6, 35]. According to many guidelines, it is recommended to wait at least 5 days after AAT discontinuation, in order to allow the INR to return to the normal range (0.80–1.20) [18–20], but this is not feasible in emergency surgery. It is interesting to note that all cases of spinal hematoma have occurred in patients with an INR in the normal range [36]. It has also been noted that warfarin's washout time is inversely proportional to the patient's age [36].

Another factor often analyzed and long debated is timing: the literature recommends that the time to surgery should not exceed 24 or 48 h, and several studies showed an increasing mortality with a longer timing, but we have to consider several possible biases [37, 38]. Strömberg et al. [39] demonstrated that there is no significant difference in the mortality for patients that underwent surgery after 72 h. Moran et al. [3] demonstrated that a delay in surgery of up to 96 h in patients without an acute medical comorbidity does not increase the postoperative morbidity, mortality, or duration of rehabilitation, but a delay of more than 4 days in patients who are fit for surgery (i.e., patients whose operation is delayed for reasons not related to their health status) significantly increases mortality [27]. On the other hand, one has to consider that the surgical delay is often related to the need for stabilization of the patient's general conditions (patients affected by comorbidities and complications), so the timing cannot be reduced [37, 40, 41].

According to the literature, there is a correlation between timing and the rate of complications after surgery

[1, 40]. Our study showed that patients on therapy with warfarin, which have a longer time to surgery than patients without anticoagulant therapy, have more complications (mainly cardiovascular diseases and infections) than other groups and a higher mortality rate than 'healthy' (i.e., patients not on AAT) patients (more than three times higher). This is probably the result of several factors, including time to surgery, forced immobilization that exposes to cardiovascular complications (thrombosis and DVT), pressure sores, and infections (mainly respiratory and urinary infections).

We found that the critical risk factors for complications in these patients are two-fold: (1) warfarin therapy and (2) excessive time to surgery. It is interesting to note that these two factors are not significant if taken alone, while they become a high-risk factor for a patient's health if taken together. In other words, a patient under warfarin therapy is at moderate risk, a patient that waits more than 5 days before operation is at moderate risk, while a patient under warfarin and whose time to surgery is over 5 days is at high risk of severe complications.

Interestingly, patients following antiplatelet therapy showed fewer complications than patients with anticoagulant therapy, even if antiplatelet and anticoagulant therapy are mainly prescribed for the treatment of the same pathologies.

Although spinal hematoma and major bleeding have been associated to warfarin and ticlopidine therapies, no increased mortality rate has been reported due to these drugs, nor any case of spinal hematoma and major bleeding has been described associated to aspirin therapy [17].

Preoperative bleeding is higher in patients under anticoagulant therapy than in patients without therapy, as we supposed, while the blood loss of patients under antiplatelet therapy was significantly lower than in warfarin patients and not significantly different from patients without therapy. However, we did not observe evidence of a higher need for RBC transfusion in group A nor in group B than in the other groups. Maybe this is due to the fact that the difference in blood loss does not always imply the need for more RBC transfusions. The treatment turned out to be an important factor in bleeding and RBC transfusion, because we demonstrated that intramedullary nailing requires more RBC transfusions than hemiarthroplasty. Morritt et al. [42] demonstrated, in a study published in 2005, that blood loss was dependent on the proposed surgical implant and it was significant higher for patients treated by intramedullary nailing, but only four patients were treated with intramedullary fixation in their study. This assertion was also supported in 2006 by Foss and Kehlet [43]. Some descriptive studies have found an association between postoperative anemia and poor functional outcome and delirium. In our study, patients treated with a hemiarthroplasty are characterized by a lower blood loss and obtain a better walking outcome compared to intramedullary nailing patients. In our opinion, this could be related to the different surgical techniques and postoperative rehabilitation, which is easier and faster for patients with a prosthesis.

Patients on warfarin therapy had a longer hospitalization than patients on AAT and longer than patients not on AAT with the same time to surgery. This is probably due to the fact that they are affected by more complications than the other groups.

Warfarin's effect can be reversed by Vitamin K administration, while aspirin and ticlopidine have no antidotes [44]. Recently, some investigators showed that Vitamin K (Phytomenadione) is very efficacious to reverse warfarin's effect (in 24–72 h) in patients on long-term oral anticoagulant therapy [6, 45–47]. Vitamin K is used by some surgical departments in order to improve drug washout—always taking into consideration the thromboembolic risk for each patient [48]. A quantity of 5–10 mg of Vitamin K may cause some problems when returning to warfarin therapy, but smaller doses, such as 1–2.5 mg, showed better and safer results [6].

Tharmarajah et al. stated that this is the safest and most efficacious method of warfarin reversal, reporting few complications which are easy to manage and without important consequences for patients. In most patients, a single administration of 1–2.5 mg of Vitamin K is adequate to reduce the INR to a normal range in less than 24 h, so surgery can be performed safely [11].

From the economic point of view, one single dose of Vitamin K has a very low price. Considering it could reduce the hospitalization by 1–2 days, this could represent an important economization for healthcare systems.

As our study shows, patients on antiplatelet therapy (by the administration of either ticlopidine or aspirin) did not show any significant differences in the postoperative blood loss, complications, and mortality compared to 'healthy' patients (i.e., patients not on therapy). This difference between patients on antiplatelet and on warfarin therapy could be biased by a lower comorbidity of these patients compared to patients on oral anticoagulation (even if the matching criteria applied to groups selection and multivariate analyses should deny this hypothesis), but maybe also to smaller systemic effects of antiplatelet agents.

## Conclusions

Elderly people on anticoagulant/antiplatelet therapy increase every year, as cardiovascular diseases prophylaxis has become commonly used, so analysis of the correct management of hip fracture (HF) patients on anticoagulant/antiplatelet therapy is very important; nevertheless, the literature is still unclear on this argument.

Our study showed that patients on oral anticoagulant therapy with warfarin are affected by higher preoperative and postoperative risks for major complications ($p = 0.009$) and mortality (odds ratio [OR] 3.63; $p = 0.055$) compared to patients under no therapy, but also compared to patients on antiaggregant therapy (AAT).

The surgeon and the patient should be warned of this higher risk related to warfarin therapy and long time to surgery; the "discontinue drug, and delay surgery" strategy usually used for patients on AAT undergoing a surgical procedure is, therefore, not suitable for patients on AAT affected by HF.

The use of Vitamin K could prove to be helpful to reduce the delay in treatment and complications and in reducing mortality and costs for healthcare system. Further studies comparing the outcomes of patients treated with the "discontinue warfarin, Vitamin K administration, and straightforward surgery" strategy versus the "discontinue drug, and delay surgery" strategy should be performed in order to confirm this statement.

*Law compliance statement* This study complies with the current laws of the country in which it was performed.

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**Conflict of interest** The authors declare that they have no conflict of interest related to this paper.

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