

**4° CONVEGNO**  
anticoagulazione.it

Attualità cliniche e di laboratorio.  
Aspetti sociali

**7-8 FEBBRAIO 2019**  
BOLOGNA Hotel Savoia Regency

EVENTO PROMOSSO DA  
fondazione **arianna**  
ANTICOAGULAZIONE

IN COLLABORAZIONE CON  
ASSOCIAZIONE  
ITALIANA  
PAZIENTI  
ANTICOAGULATI  
BOLOGNA

EVENTO SENZA FINI DI LUCRO

SESSIONE 1

Gli studi della Fondazione Arianna Anticoagulazione (FAA), l'attività di START2-Registry

**ORTHO-START**

**Elvira Grandone (San Giovanni Rotondo, FG) e Angelo Ostuni (Bari)**

Angelo Ostuni

**Blood Risks**

**Blood Appropriateness**

**Blood Safety**

- Avoid/treat infections promptly
- Be aware of adverse effects of medication

Fig 1 A multimodal approach to PBM (or blood conservation). Adapted from Hofmann and colleagues<sup>62</sup> with permission, ESA, erythropoiesis stimulating agents.

**Perioperative measures**

Before operation, PBM involves a careful assessment of bleeding risk and anaemia well in advance of surgery (e.g. 30 days) to allow full evaluation and correction of anaemia. This has been specifically recommended in patients undergoing orthopaedic surgery.<sup>63</sup> The patient's own blood should be conserved by restricting blood drawn for tests and by restricting the use of antiplatelet and anticoagulant agents to situations where these drugs are indicated. Pharmacological and mechanical venous thromboembolism prophylaxis measures are both widely used in patients undergoing THR and TKR, with recommendations of better compliance with established evidence-based guidelines.<sup>64</sup> Autologous preoperative donation was once promoted to decrease the need for ABT. However, predonated blood is also subject to storage lesion, and is labour intensive, expensive, and inefficient, with almost half of predonated autologous units not used.<sup>65</sup> Some patients may not be able to predonate blood due to comorbidities and current or potential anaemia.<sup>6</sup>

There are possible deleterious effects of blood units predonated weeks ahead of surgery.<sup>66</sup> It has been suggested that Hb levels before orthopaedic surgery should be within the normal range (the World Health Organization (WHO);  $\geq 12$  g dl<sup>-1</sup> in men).<sup>61</sup> Iron supplementation should be used to correct iron deficiency. Oral iron is effective in need for transfusion before orthopaedic surgery.<sup>67</sup> Erythropoiesis-stimulating agents (ESAs) may be added in patients with preoperative anaemia. A prospective, non-randomized case series suggests that iron can correct iron deficiency anaemia before orthopaedic surgery<sup>67</sup> and reduce rates of ABT, infection, and mortality in patients with hip fracture compared with historical controls.<sup>68, 69</sup> Another study found that the perioperative use of i.v. iron with ESA therapy in anaemic patients with hip levels of  $< 13$  g dl<sup>-1</sup> reduced the proportion requiring transfusion, the number of units transfused.

British Journal of Anaesthesia 109 (1): 55-68 (2012)  
**Patient blood management in Europe**  
A. Shander et al.

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Angelo Ostuni

**SAVE BLOOD, SAVE LIVES – Emily Anthes - NATURE vol. 520, 2 April 2015**  
*Transfusions are one of the **most overused** treatments in modern medicine, at a cost of billions of dollars.*



**DOCTOR'S ORDERS**  
By simply reminding doctors of the current guidelines when they order blood, a California hospital was able to save money and lives.



Reducing the blood used for transfusions by nearly one-quarter saved the hospital US \$1.6 million per year.

The average length of stay for patients who received transfusions went from 10.1 days to 6.2.

Mortality among people who had transfusions fell from 5.5% to 3.3%.

Photograph by Greg White

Angelo Ostuni

**ANESTHESIOLOGY**   
The Journal of the American Society of Anesthesiologists, Inc.

**From: Perioperative Management of Elderly Patients with Hip Fracture**  
Anesthes. 2014;121(6):1336-1341. doi:10.1097/ALN.0000000000000478



**Beyond 70 years = 5 comorbidities**

**Frequency of main comorbidities in the elderly patients.**

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Angelo Ostuni


**THE SCALE OF THE PROBLEM DATA COLLECTION (1)**

**Orthopaedic surgeons make high demands on blood banks.**

**USA:** ... 300,000 people sustain a hip fracture... → an explosion in the amount of elective orthopaedic work.

**United Kingdom:** ...100,000 hip and knee arthroplasties were performed with perhaps half of these patients receiving allogenic blood.

**Estimated blood loss, age, weight, aspirin or AVK or NOACs use are all indicators but by far the strongest predictor of the need for transfusion is the preoperative Hb level. Whenever this falls in the range of 10 ÷13 g/dl the patient has a significantly higher risk of requiring allogenic blood.**



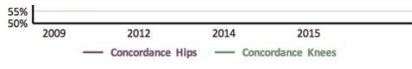
”

THE REAL QUESTION IS NOT WHETHER A TRANSFUSION WAS APPROPRIATE.

THE REAL QUESTION IS WHETHER A TRANSFUSION WAS AVOIDABLE.

ARYEH SHANDER, MD

**Patient blood management strategies in total hip and knee arthroplasty**  
Christopher Newman et al. - Current Orthopaedic Practice 2018



**FIGURE 3.** (A) Percentage of blood transfusions for hip arthroplasty (purple) and knee arthroplasty (green) for years 2009-2015. (B) Percentage of the patients transfused for hip arthroplasty (purple) and knee arthroplasty (green) in adherence with national blood transfusion guidelines for years 2009-2015.

also significantly reduced hospital costs. With respect to management of anemia, which broadly includes educational transfusion... Champion *et al.*<sup>33</sup> implemented educational transfusion... of our findings suggest that improvements can be in patient blood management by taking on the recommend

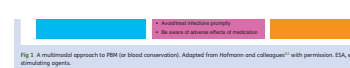


Fig 3 A multimodal approach to TBM (or blood conservation). Adapted from Helfman and colleagues<sup>33</sup> with permission. ESA, or stimulating agents.

**Perioperative measures**

Before operation, PBM involves a careful assessment of bleeding risk and anemia level in absence of surgery (4 to 10 days) to allow full evaluation and correction of anemia. This has been specifically recommended in patients undergoing orthopaedic surgery.<sup>34</sup> The patient's own blood should be conserved by restricting blood drawn for tests and by restricting the use of antiplatelet and anticoagulant agents to situations where these drugs are indicated. Pharmacological and mechanical venous thromboembolism prophylaxis measures are both widely used in patients undergoing THR and TKR, with recommendations of better compliance with established evidence based guidelines.<sup>35</sup> Autologous preoperative donation was once promoted to decrease the need for ABT. However, predonated blood is also subject to storage lesions, and is labour intensive, expensive, and inefficient, with almost half of predonated autologous units not used.<sup>36</sup> Some patients may not be able to predonate blood due to comorbidities and current or potential anaemia.<sup>37</sup>

There are possible deleterious effects of blood units predonated weeks ahead of surgery.<sup>38</sup> It has been suggested that Hb levels before orthopaedic surgery should be within the normal range (the World Health Organization (WHO) >12 g/dl >13 g/dl in men)<sup>39</sup> Iron supplementation or to correct iron deficiency. Oral iron is effective in need for transfusion before orthopaedic surgery.<sup>40</sup> Erythropoiesis-stimulating agents (ESA) may be added in patients with preoperative anaemia. In a prospective, non-randomized case series, surgery can correct iron deficiency anaemia, but orthopaedic surgery<sup>41</sup> and reduce rates of ABT, infections, and mortality in patients with hip arthroplasty compared with historical controls.<sup>42</sup> Another study found that the perioperative use of iron with ESA therapy in anaemic patients with Hb levels of <13 g/dl<sup>43</sup> reduced the proportion requiring transfusion, the number of units received.

**Abstract**

The number of hip fractures in anticoagulated patients is predicted to increase people living longer. However, evidence regarding urgent postoperative management of elderly patients with hip fracture who take oral anticoagulants (vitamin K inhibitors or direct oral anticoagulants) is scarce. In this article, the authors present a narrative review of the evidence for safe stopping the agent management fracture in anticoagulated elderly patients. They discuss the complexity of the high risk of procedure-related bleeding and, at the same time, the high thromboembolic risk. The role of a bridging procedure and the best strategy to manage it are also reviewed. Further studies are required to improve evidence in urgent surgery, especially in frail elderly patients.

**Keywords**

- anticoagulants
- hip fracture
- vitamin K
- thromboembolism
- heparin
- bridging
- emergencies

The number of patients taking oral anticoagulants, including vitamin K antagonists (VKAs) and non-vitamin K antagonists oral anticoagulants (NOACs), has dramatically increased in the last decades. Due to the higher rates of falls and, therefore, to an increased number of patients with oral fibrillation. As a consequence, the number of invasive procedures or surgery in anticoagulated patients is growing steadily and is predicted to increase further. It has been calculated that annually 150,000 patients taking oral anticoagulants need treatment interruption for surgery or invasive procedures. Elderly patients, especially those with multiple health impairments, are at risk for falls and fractures of the hip, femur, and other bones that usually result from the combined effect of falls and osteoporosis. Approximately 75,000 proximal hip fractures occur in the United Kingdom annually. The incidence of hip fracture increases with the highest incidence of hip fractures, has rates of over 300 per 100,000 in women and over 150 per 100,000 for men.<sup>1</sup>

The management of patients taking VKAs or NOACs needs to take into account (1) stratification of patient-related and procedure-related risks of thrombosis and bleeding (2) withdrawal and resumption of anticoagulation according to the pharmacokinetics properties of each agent.

**Methods**

We reviewed publications focused on the management of patients taking oral anticoagulants who need urgent surgery or invasive procedures. We searched on Medline, Embase, Scopus, and Cochrane Central Register of Controlled Trials. We included articles using a combination of the following keywords: "anticoagulation", "oral anticoagulants", "vitamin K antagonists", "non-vitamin K oral anticoagulants", "warfarin", "direct oral anticoagulants", "NOACs", "bridging", "heparin", "bivalirudin", "hyaluronidase", "protamine", "factor Xa inhibitors", "thrombolytics", "thrombolysis", "thromboembolic risk."

**Conclusion**

The management of patients taking VKAs or NOACs needs to take into account (1) stratification of patient-related and procedure-related risks of thrombosis and bleeding (2) withdrawal and resumption of anticoagulation according to the pharmacokinetics properties of each agent.

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a) The **number of patients taking oral anticoagulants, including vitamin K antagonists (VKAs) and non-vitamin K antagonist oral anticoagulants (NOACs), has dramatically increased** in the last decades,

b) the **number of invasive procedures or surgery in anticoagulated patients is growing steadily** and is predicted to increase further. It has been calculated that annually 10% to 15% of patients taking oral anticoagulants need treatment interruption for surgery or invasive procedures

c) Approximately **77,000 proximal hip fractures** occur in the United Kingdom annually, whereas **Italy has rates of over 300 per 100,000 for women and over 150 per 100,000 for men**

•Steinberg BA, Peterson ED, Kim S, et al., *Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) investigators and patients. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)*. Circulation 2015

•National UK Report - [http://www.ccad.org.uk/nhfd.nsf/NHFD\\_National\\_Report\\_2010.pdf](http://www.ccad.org.uk/nhfd.nsf/NHFD_National_Report_2010.pdf)

•White SM, Griffiths R, Holloway J, Shannon A. *Anaesthesia for proximal femoral fracture in the UK: first report from the NHS Hip Fracture Anaesthesia Network*. Anaesthesia 2010

•Kanis JA, Odén A, McCloskey EV, Johansson H, Wahl DA, Cooper C. *A systematic review of hip fracture incidence and probability of fracture worldwide*. Osteoporos Int 2012

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The number of hip fractures in anticoagulated patients is predicted to increase people living longer. However, evidence regarding urgent postoperative management of elderly patients with hip fracture who take oral anticoagulants (vitamin K inhibitors or direct oral anticoagulants) is scarce. In this article, the authors present a narrative review of the evidence for safe stopping the agent management fracture in anticoagulated elderly patients. They discuss the complexity of the high risk of procedure-related bleeding and, at the same time, the high thromboembolic risk. The role of a bridging procedure and the best strategy to manage it are also reviewed. Further studies are required to improve evidence in urgent surgery, especially in frail elderly patients.

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**Cumulative mortality at 12 months:**  
**37,1% in men and 26,4% in women with hip fracture**

a) **post-operative complications** and underlying medical conditions following fracture (pulmonary embolism, heart failure, and infection)

b) **pre-operative predictors:** duration between injury and surgery

c) **early surgery is associated with better outcome** in terms of mortality and morbidity, decreased hospital stay, less pain, and a reduction in major complications

**Overall incidence of asymptomatic DVT: 28%**

European and American guidelines recommend pharmacological DVT thromboprophylaxis with heparins, fondaparinux, VKAs, or NOACs and/or mechanical thromboprophylaxis for elective hip/knee arthroplasty and emergency hip fracture

**Hip arthroplasty is associated with clinically relevant peri-operative blood loss**



**START-ORTOPEDIA**  
**CHIRURGIA ELETTIVA ED IN EMERGENZA (PROTESI ANCA-  
GINOCCHIO; FRATTURA FEMORE) IN PAZIENTI ANTICOAGULATI**

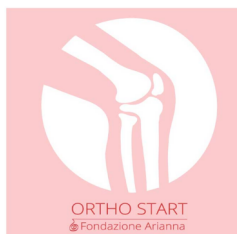
Scopo: contribuire al miglioramento della gestione peri-operatoria nel paziente fragile come il paziente anziano con pluripatologie e plurimedicato, con l'obiettivo di ridurre le complicanze e la mortalità a breve e medio termine .

Tipo di studio:

studio osservazionale, prospettico, di coorte, multicentrico, nazionale, no profit.

Metodo:

1. Registrazione dei dati relativi alla **gestione peri-operatoria di pazienti in terapia anticoagulante e/o antiaggregante che necessitano di intervento elettivo di protesi d'anca/ginocchio o frattura del femore**
2. Registrazione delle **complicanze**
3. Blood Management



## Un po' di numeri....

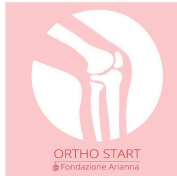


- 77.000 fratture femore/anno in UK (White SM, Anesthesia 2010; 65: 243-8)
- Italia: uno dei Paesi con la più alta incidenza di fratture femore **300 per 100000 donne e > 150 per 100000 uomini** (Kanis JA, Osteoporos Int. 2012)
- La gestione dei pazienti in AVK o DOAC deve essere definita in base a:
  - a) stratificazione dei rischi correlati al paziente e correlati alla procedura di trombosi e sanguinamento;
  - b) le conseguenze cliniche di un evento trombotico o emorragico;
  - c) interruzione e ripresa della terapia anticoagulante in base alle proprietà farmacocinetiche di ciascun farmaco.

## ASPETTI DA CONSIDERARE



- Fattore tempo (Chirurgia entro 48 ore)
- Rischio di Tromboembolismo Venoso (Falck-Ytter Y, Chest. 2012 ][Abelseth G, J Orthop Trauma. 1996)
- Necessità di profilassi con Eparine o Fondaparinux o con DOACs (Forster R., Cochrane Database Syst Rev. 2016)
- Rischio emorragico
- Intervenire in sicurezza dopo aver «compensato» il potenziale emorragico delle terapie con anticoagulanti (sia AVK che Inibitori diretti DOACs...)
- Anemia: come trattarla/prevenirla, Trasfondere come, quando e quanto.



**Endpoint primari**

1. Registrazione di eventi tromboembolici venosi o arteriosi (incluso ictus, infarto miocardio, embolie arteriose periferiche)
2. Sicurezza dei trattamenti relativamente al verificarsi di complicanze emorragiche o di altra natura: emorragie maggiori o non maggiori ma clinicamente rilevanti, ed eventuale comparsa di altre manifestazioni morbose.
3. Gestione e prevenzione dell'anemia nel periodo peri-operatorio.

**Endpoint secondari**

1. Analisi delle caratteristiche dei possibili diversi schemi di sospensione e ripresa del trattamento anticoagulante
2. Valutazione del numero di unità di emocomponenti somministrati in funzione della gravità dell'anemia e confronto di soglie trasfusionali rispetto ad end-point di efficacia e sicurezza



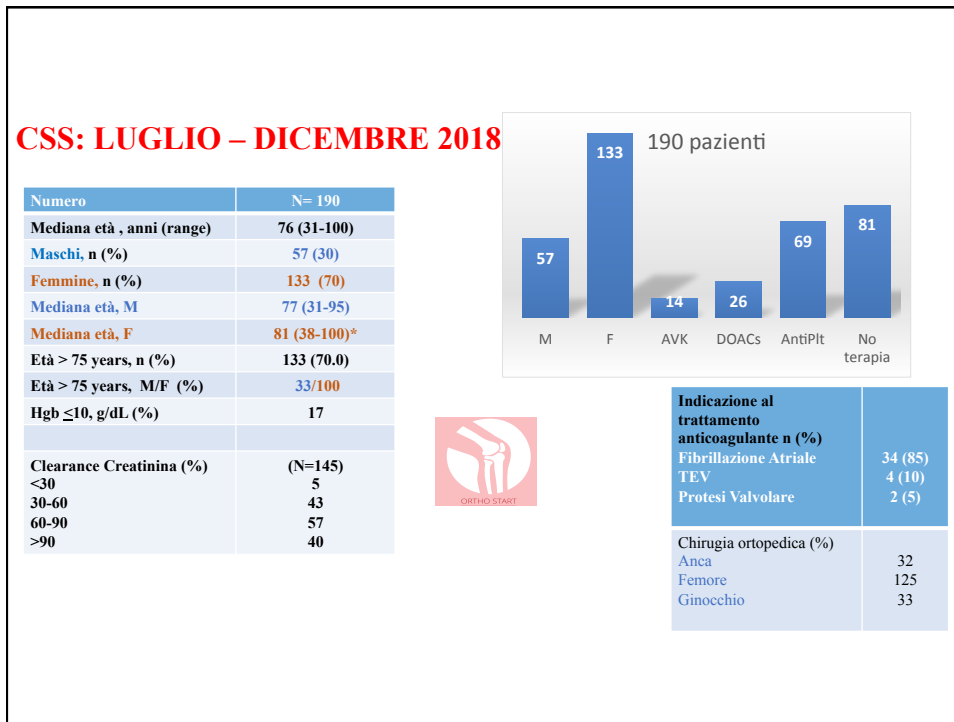
**ORTHO-START**

**CHIRURGIA ELETTIVA ED IN EMERGENZA (PROTESI ANCA-  
GINOCCHIO; FRATTURA FEMORE) IN PAZIENTI ANTICOAGULATI**

Scopo generale: osservazione e registrazione dei dati relativi alla gestione peri-operatoria e alle complicanze in pazienti trattati con farmaci anticoagulanti e/o antiaggreganti per contribuire al miglioramento della gestione del paziente fragile come il paziente anziano con pluripatologie e plurimedcato, al fine di ridurre le complicanze e la mortalità a breve e medio termine.

***AD OGGI: 15 CENTRI HANNO INVIATO SCHEDE DI  
ADESIONE***

[e.grandone@operapadrepio.it](mailto:e.grandone@operapadrepio.it)



**TRASFUSIONI**  
Totale pazienti: 49 (25.8%)

Trasfusioni	N (%)	> 75 anni N	FF N (%)	Anticoag/ Antiplt
Pre-op	14	13	13 (93)	4/3
Intra-op	2	2	2	1/1
Post-op	33	27	28 /33 (84.8)	7/11



**«NON E' MAI TROPPO TARDI PER COMINCIARE A CORRERE SE HAI QUALCUNO ACCANTO...»**



**Prof. G. PALARETI**  
Presidente **FONDAZIONE ARIANNA**



**Dott. A. OSTUNI**  
Responsabile Struttura Regionale di  
Coordinamento Attività Trasfusionali Regione  
Puglia e Responsabile Struttura Complessa  
Medicina Trasfusionale, AOU Policlinico di Bari.



**Dott.ssa E. ANTONUCCI**  
Comitato di Redazione  
Fondazione Arianna  
[www.ariannafoundation.org](http://www.ariannafoundation.org)





**Prof. F. MARONGIU**  
Prof Ordinario Medicina Interna,  
Università degli Studi di Cagliari  
Dipartimento di Scienze Mediche  
Internistiche, Cagliari



