Medico economic evaluation of oral Iron supplementation in Major Surgeries, a French Nationwide Healthcare Database Study

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INTRODUCTION

Anemia is frequent in patients scheduled for major surgeries, affecting around a third of them.

Both anemia and blood transfusion are associated with poorer outcomes in surgical patients.^{1–3} This led to the development of the concept of patient blood management in the past two decades.

Correction of preoperative iron deficiency and anemia is widely recommended.

METHODS



Study design

Retrospective comparative cohort study between patients treated with Oral iron versus patients not treated with iron using SNDS data (the main French

national health database) was carried out.

Patients

- All patients who underwent major surgeries (orthopedic, oncologicaldigestive, cardiac, oncological-gynecological, oncological-urological surgeries) between January 2017 and September 2019 were eligible.
- Patients were separated in 2 groups, depending on whether they received

Statistical analyses

- Baseline characteristics were described by standard statistical analyses
- Unadjusted and adjusted matched, conditional logistic regression models were used to evaluate PMM risk.
- -The adjustment set comprised of sex, age (years), preoperative folic acid supplementation, preoperative erythropoiesis-stimulating agent (ESA) supplementation, Rey deprivation index, Charlson score, obesity, and the annual volume of activity of the establishment in surgery at risk of bleeding.

However, whether preoperative oral iron
 supplementation improves postoperative outcomes
 after high-risk hemorrhagic surgery remains
 unknown.

OBJECTIVES

This study evaluates the benefits of oral iron supplementation given before major surgeries (in 5 areas) on Postoperative Morbi-Mortality (PMM) and the associated costs. oral iron within 8 weeks prior to surgery (oral iron group) or not (no iron group).

Outcomes

Outcome 1:

> PMM were defined as re-hospitalization, venous thrombo-embolism (VTE), infection, stroke/myocardial infarction, unplanned admission to intensive care unit (ICU), renal insufficiency, and postoperative death occurring within 90 days following surgery (POD90).

Outcome 2:

The cost of managing complications avoided by oral iron treatment in patients who have undergone major surgery was estimated based on the number of morbidity and mortality cases avoided per 1,000 surgeries with oral iron supplementation and the cost of managing these complications.

-For matching analyses, patients were matched on the type of surgery and the following anemia risk factors: age (>65 years), gender, anemic digestive cancer, chemotherapy-induced anemia, chronic inflammatory disease, chronic renal failure, long-term treatment with anticoagulants/antiaggregants, gastrointestinal bleeding in the past 6 months, and malabsorption syndrome within the last 6 months (1 oral iron group for 4 no iron group).

The cost of managing complications avoided by oral iron supplementation was evaluated by type of event using unadjusted and adjusted linear regression

RESULTS

Population (Figure 1)

A total of 947,468 patients who underwent 975,852 surgeries were included (28,384 [3.0%] patients underwent two surgeries).



1st Outcome (Figure 2) (continued)

- > These was particularly true for:
- VTE occurrence (OR=0.84, 95% CI [0.80-0.87]),
- Infection (OR=0.93, 95% CI [0.90-0.97]),
- ICU admission (OR=0.90, 95% CI [0.84-0.96]), and
- Death (OR=0.91, 95% CI [0.83-0.99]) (p<.04)

- > Of these 975,852 surgeries:
- 7.1% (69,377) received oral iron supplementation within
 8 weeks prior to surgery.
- 0.5% (4,582) received intravenous iron supplementation were not included in the analyses.

Baseline characteristics

- The mean (SD) age was 68.2(11.8) years in the no iron group and 68.3(13.6) in the oral iron group
- Women were predominant in both groups (55.3% and 72.1% respectively) with a higher proportion in the oral iron group (p<.001).</p>
- Patients in oral iron group were older, with higher obesity, a higher number of anemia risk factors, more vitamin B12, folic acid and Erythropoietin (EPO) supplementation (p<.001), but they had a lower Charlson score (p<.001)</p>

1st Outcome (Figure 2)

Solution Oral iron group's patients had less post-operative morbimortality than no iron group's patients (23.7% vs. 24.2%, p<.001).</p> -Haemopathy, haemochromatosis, haemolytic anaemia, bone marrow aplasia or other anaemia **N=136,299**

Surgeries included N= 975,852 Oral iron n= 69,377 (7,1%) Intravenuous iron * n= 4,582 (0,5%) No iron= 901, 893 (92.4%)

Figure 1. Study Flowchart

Death within 90 days of surgery

Morbi-mortality		OR [95% CI]		p-value
Occurrence of peri- and post-operative morbidity and mortality	Unadjusted	0.94 [0.92 ; 0.96]	Her	<.001
within 90 days of surgery	Adjusted	0.93 [0.91 ; 0.95]		<.001
Re-hospitalization within 90 days of surgery	Unadjusted	1.04 [1.01 ; 1.06]	H	0.010
	Adjusted	1.00 [0.97 ; 1.03]	HEH	1.000
VTE (venous thromboembolism) within 90 days of surgery	Unadjusted	0.85 [0.81 ; 0.88]	H	<.001
	Adjusted	0.84 [0.80 ; 0.87]		<.001
Renal failure of 90 days of surgery	Unadjusted	1.04 [0.96 ; 1.13]	-	0.296
	Adjusted	1.01 [0.93 ; 1.10]		0.808
Infection within 90 days of surgery	Unadjusted	0.92 [0.89 ; 0.96]	H	<.001
	Adjusted	0.93 [0.90 ; 0.97]		<.001
Stroke/myocardial infarction within 90 days of surgery	Unadjusted	0.92 [0.76 ; 1.11]	⊢	0.375
	Adjusted	0.86 [0.70 ; 1.07]		0.166
Intensive care unit admission within 90 days of surgery	Unadjusted	0.92 [0.87 ; 0.98]		0.007
	Adjusted	0.90 [0.84 ; 0.96]		0.002

2nd Outcome (Table 1)

Table 1 shows the average cost difference according to the different complications and the estimated savings for 1000 surgeries.

For VTE, the average cost difference was higher for patients without VTE compared to patients with VTE. No average cost avoided with oral iron supplementation was estimated for VTE.

Table 1: Average total costs (€) in the 90 post-operative days of the various morbidity and mortality; number and average cost avoided per 1,000 surgeries if preventive treatment with oral iron is used

Postoperative Morbi- mortality (PMM)		Average cost difference (€)* (with PMM -without PMM)	95% CI	P-value	
VTE		-549.89	[-598.86 ;500.92]	<0.01	
Infections (including pneumopathy)		4670.54	[4624.98 ;4716.10]	<0.01	
ICU admission		6854.36	[6775.60;6933.13]	<0.01	
Death		660.58	[552.83;768.33]	<0.01	
Postoperative Morbi- mortality	Num cases if pre iron*	ber of morbidity and mortality s avoided per 1,000 surgeries ventive treatment with oral *.	Average cost avoided per 1,000 surgeries if preventive treatment with oral iron (€)***		
VTE		Not perform	Not perform		
Infections (including pneumopathy)		2	9 341.08		
ICU admission		2	13 708.72		
Death		0	0		

They had a lower adjusted PMM risk (OR=0.93, 95% CI [0.91–0.95], p<.001 using a matched analysis on anemia risks factors).



Figure 2. results of conditional unadjusted and adjusted* logistic regression with matched** population: N=344, 879 1:4; (69, 351 + 275, 528).

*Adjustment: Preoperative folic acid supplementation; Preoperative erythropoiesis-stimulating agent (ESA) supplementation; Sex (not in matched data analyses); Age (in years); Rey deprivation index (quintile) of municipality of residence; Charlson score; Obesity declared during hospitalization in the 6 months preceding surgery; Annual volume of activity of the establishment in surgery at risk of bleeding.

**Analysis was performed with patient matching on the type of surgery and anemia risk factors. Each surgery on a patient supplemented with oral iron was matched with a surgery on a patient without iron supplementation and with 9 identical anemia risk factors, namely: age (>65 years), gender, anemic digestive cancer, anemia-inducing chemotherapy, chronic inflammatory disease, chronic, renal failure, long-term treatment with anticoagulants / antiaggregants, gastrointestinal bleeding in the past 6 months, malabsorption syndrome within the last 6 month

ICU:intensive care unit PMM: Postoperative Morbimortatlity; VTE: venous thrombo-embolism

*Difference obtained using linear regression models adjusted for sex, age, Rey deprivation index (quintile) for the municipality of residence, oral iron supplementation, other anaemia treatments apart from oral iron, type of surgery, Charlson score, obesity declared during hospitalisation in the 6 months preceding surgery and the volume of activity of the establishment in surgery at risk of haemorrhage, as well as by the occurrence of different morbidity and mortality in the 90 days following surgery.

** VTE rate: 5.50% without iron and 4.59% with iron Rate of infections (including pneumopathies): 7.10% without iron vs 6.89% with iron Rate of admission to intensive care unit: 2.30% without iron vs. 2.13% with iron Death rate: 1.17% without iron vs 1.17% with iron

*** Average cost avoided per 1,000 surgeries if preventive treatment with oral iron =Difference in average cost (€) Multiplied by Number of morbiditymortalities avoided per 1,000 surgeries if preventive treatment with oral iron

CONCLUSION

In this real-life cohort, oral iron supplementation within 8 weeks before major surgery is associated with less PMM within POD90 than that with no iron supplementation.

Oral iron supplementation was associated with average cost avoided for infections and ICU admission, but no evidence of cost avoided regarding the death or VTE.

VTE results could be explained by interactions with the other PMMs in estimating the average cost difference, meaning that one or more other complications could modify the average cost difference for VTE when patients have VTE and other PMMs.

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