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ORIGINAL PAPER

Use of a fibrin sealant within a blood-saving protocol in patients undergoing revision hip arthroplasty: effects on post-operative blood transfusion and healthcare-related cost analysis

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Abstract

Purpose Blood transfusion and blood management are important aspects in orthopaedic surgery. Strategies include intra-operative and post-operative blood salvage and even the use of fibrin sealant in selected case. Objectives of the study were (1) to compare the total number of transfusions and the length of hospital stay in patients undergoing complete revision hip arthroplasty (RHA) with and without the use of a fibrin sealant (EVICEL®) and (2) to evaluate the possible role in cost savings of EVICEL® in association with the blood-saving protocol.

Methods Retrospective observational study evaluating patients undergoing complete RHA (stem + cup) with a blood-saving protocol with ($n = 50$) and without EVICEL® ($n = 60$). The outcome measures were: number of patients transfused (allogeneic red blood cells—RBC—and plasma), amount of blood/plasma transfusions, quantity of re-infused recycled blood, and length of hospital stay. An economic model was developed to assess the differences in costs between the two groups.

Results EVICEL® reduced the number of transfused red blood cells and plasma ($p < 0.001$), and the hospital stay ($p = 0.01$) compared to control group. EVICEL® can induce a reduction in resource consumption with an average cost-savings of €1.676 per patient.

Conclusion EVICEL® may be effective in reducing red blood cells and plasma transfusion as well as hospital stay. The inclusion of EVICEL® in a blood-saving protocol seems to produce clinical efficacy and cost savings.

Keywords Total hip arthroplasty · Revision · Blood management · Transfusion · Fibrin sealant · Evicel

Abbreviations

ASA	America Society of Anesthesiologists
BMI	Body mass index
GCP	Good clinical practice
Hb	Haemoglobin
HCV	Hepatitis C virus
PSI	Pound per square inch
RHA	Revision hip arthroplasty
TKR	Total knee replacement
RBC	Red blood cells
ROM	Range of motion

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Introduction

Elective orthopaedic surgery, in particular joint reconstruction and revision procedures, can lead to significant intra- and post-operative blood loss [1–3] with the consequent need of allogenic blood transfusions. This is even more true when caring for patients with multiple associated conditions or on anticoagulant drugs, who can face increased risk of anaemia, post-operative infections, prolonged hospital stay, and increased healthcare costs [2, 4–6]. Allogenic blood

transfusions are known to be associated with significant risk of infective organism transmission, transfusion and allergic reactions, and post-operative surgical site and systemic infections [1, 2, 4, 5, 7, 8]. Moreover, the availability of blood and blood derivatives can be sometimes reduced.

For these reasons, blood-saving protocols to reduce allogenic transfusion for high-risk patients undergoing total hip and knee arthroplasties and revisions have been established. These protocols include pre-operative autologous blood donation, acute normovolemic haemodilution, hypotensive anaesthesia, blood-saving oriented-surgical procedures, subcutaneous placement of a vacuum drain, strict application of post-operative haemorrhagic management, and the administration of parenteral iron and erythropoietin [9–11].

EVICEL® Fibrin Sealant (Johnson & Johnson Wound Management, Ethicon, Somerville, NJ, USA) is a fibrin sealant that contains a concentrate of human clottable fibrinogen and human thrombin containing calcium. EVICEL® is currently indicated as an adjunct for hemostasis in patients undergoing surgery where standard surgical techniques are insufficient [12]. It has been recently suggested that the use of EVICEL®, alone or in combination with pre-operative autologous blood donation, may reduce the need for allogenic transfusion after knee arthroplasty. Moreover, the use of fibrin sealant resulted in a significant reduction of blood loss compared to pre-operative autologous blood donation only [13].

In 2012, EVICEL® was introduced as part of the blood-saving protocol used in our Institution for all patients undergoing hip and knee replacement procedures with coagulation disorders, HCV-related liver diseases, on anticoagulant drug therapy, or in patients candidate for complex procedures, such as revisions of prosthetic implants.

The aim of this retrospective study was to evaluate if the addition of EVICEL® to the standard blood-saving protocol may reduce the need for allogenic blood and/or plasma transfusion in patients undergoing complete revision hip arthroplasty (i.e., concurrent stem and cup revision), and if its introduction may be associated with a reduction in procedure-related costs.

Methods

Ethical statement

A retrospective, observational study was performed to verify if the use of EVICEL® within the blood-saving protocol may reduce the need for post-operative blood/plasma transfusions for patients undergoing complete revision hip arthroplasty (RHA) in comparison to the standard protocol without EVICEL®. The study protocol was notified to Humanitas Research Hospital (ICH) Ethical Committee. During the study, the data were collected in complete anonymity and handled according to the local law on privacy. The ICH blood management protocol is compliant with the Declaration of Helsinki, to the standards EN ISO 14155:1, EN ISO 14155:2 and Good Clinical Practices (GCP). Moreover, all personnel involved in the study agreed to act in accordance with the principles contained in these GCPs.

Patient selection

The clinical records of patients who underwent any kind of hip revision surgery since the adoption of the fibrin sealant were collected. A total of 147 patients in total were found, and 93 of them were excluded because they did not undergo complete revision of the implant. Therefore, 54 patients who underwent concurrent stem and cup revision were screened: three of them did not have complete dataset for the purpose of the present study, and one had refused to give consent to use his clinical data for research purpose. Thus, 50 patients in total were included in the final data analysis. Based on a post hoc power analysis (described in the "Statistical analysis" Subsection), we needed to include at least 49 patients in the study group, and therefore, our cohort of 50 patients was sufficient for statistical evaluation. This group of patients was matched and compared to another group of 60 patients previously operated of complete RHA without the addition of the fibrin-sealant.

The clinical criteria for the use of fibrin sealant were agreed among orthopedic surgeons, anesthesiologists, and internal medicine specialists of our Institute and were (1) patients candidate to prosthetic hip revision; (2) no concurrent bone grafting or other associated surgical procedures; (3) ≥ 50 and < 80 years; (4) body weight ≥ 50 and < 90 kg; (5) haemoglobin (Hb) levels > 12 g/dL for males and > 11 g/dL for females; (6) ferritin levels > 80 ng/mL; exclusion criteria were (1) hypersensitivity to the active substances or to any of the excipients of EVICEL®; (2) creatinine clearance < 30 mL/min; (3) American Society of Anesthesiologists (ASA) class 4.

All surgical procedures were performed by the same surgical staff with the adoption of standardized blood-saving techniques. These included hypotensive loco-regional anesthesia, side-lying position with the limb to be operated facing up, conscious sedation with administration of midazolam and continuous infusion of low doses of remifentanyl, heating devices, and administration of tranexamic acid (10 mg/kg intra-operatively). RHA was performed according to standard surgical technique [14].

Evicel® application and post-op care

Patients operated with the use of EVICEL® 5 mg were given 10 mL of EVICEL®, composed of human-derived fibrinogen (from 250 to 450 mg) and thrombin (4000–6000 IU) in two separate vials (5 mL each). The two vials were thawed and combined in a 1:1 ratio for application and sprayed over

tissues using the corresponding fibrin sealant double syringe. The recommended CO_2 pressure for spraying using this device was 20–25 PSI (1.4–1.7 bar) at a distance of 10–15 cm. In particular, after the prosthesis had been inserted, the intra-articular space and the entire operative field was rinsed of any debris and was meticulously dried. EVICEL® was then applied after closing the capsule and before closing the fascia by topical spraying over the soft tissues, in order to cover as much surface as possible with the film of glue. The application of the fibrin spray was performed in the final stages of the procedure because the thin layer derived from application might have been altered from lavages and swabs.

A blood recycling device was placed in all patients. This device allowed to re-infuse the re-collected blood mostly devoid of its supernatant. The device recycled and reinfused blood for no more than six hours post-operatively and no more than 700 mL [15]. These limits were introduced to avoid alterations in haemostasis, to limit the inflammatory process, and to avoid excessive reinfusion of recycled supernatant. Furthermore, in the post-op, all patients were administered 1 g of ferric carboximaltose intra-venously.

Allogenic blood transfusion was allowed if Hb levels fell below 6 g/dL in ASA (American Society of Anesthesiology) class 1 and 2 patients, 7 g/dL in ASA 3 patients, and 9 g/dL for ischemic but stable patients. Plasma was transfused if more than four blood units were transfused or if coagulation parameters were out of acceptable range. The prescription of blood or plasma transfusions was allowed only to the ward doctor or the anaesthesiologist responsible for the surgical procedure. When transfusion was indicated, 1 unit of packed red blood cells (RBC) was transfused at a time to increase Hb levels to 8.0 g/dL in ASA 1–3 patients. Autologous blood transfusion was performed using the same thresholds if autologous blood was collected pre-operatively. All patients underwent prophylaxis following both the American College of Chest Physicians [16] and the International Consensus Statement [17] guidelines for the prevention of symptomatic deep venous thrombosis (DVT) or pulmonary embolism (PE).

Outcome measures

All clinical information was retrospectively collected from the clinical records of the patients and maintained in a database. The clinical information included gender, age, BMI, number of autologous transfusions, number of allogeneic transfusions, number of plasma transfusions, and length of hospital stay.

The cost benefit ratio was calculated considering the average cost of an autologous or allogeneic unit of blood and plasma, the cost of EVICEL®, and the cost of each hospital day according to the Italian hospital perspective. All blood derivatives and units of red blood cell (RBC) costs were calculated net of transfusion center costs. The costs related to hospital stay were evaluated on the basis of total costs of an average hospitalization for the disease, as retrieved from the management of the hospital. The cost of EVICEL® was calculated on the basis of the price paid by the hospital for each sample of the device.

The economic evaluation consisted in a cost and budget impact analyses of the adoption of EVICEL® into the blood-saving protocol. These data were then compared with historical data before the use of EVICEL® to verify possible savings.

The primary end points of the study were: difference in total (RBC and plasma) transfusion rate, RBC transfusion rate, and plasma transfusion rate between the group treated with EVICEL® and the group not treated with EVICEL®. Secondary endpoints were difference in number of allogenic or autologous blood and plasma transfusions, length of hospital stay, reinfused blood volumes, and costs between the two groups.

Statistical analysis

Considering a two tailed alpha error of 5%, and a power of 80% to detect a difference from 75 to 50% of transfusion (RBC + plasma) rate between the two treatment groups, it was calculated that a total amount of 98 patients (49 per group) were needed for inclusion. After the retrospective analysis, 50 patients in the EVICEL® group and 60 patients in the control group were included and analyzed.

Statistical analysis was performed using STATA release 12 (StataCorp, College Station, TX, USA). Distribution of continuous data was evaluated using the Shapiro-Wilks test. Age, height, weight, and body mass index (BMI) showed a normal distribution, and differences between groups were analyzed using the Student's t test for uncoupled samples. Number of RBC and plasma units transfused and length of hospital stay displayed a non normal distribution and the Mann-Whitney test was used to evaluate differences between groups. Differences in categorical variables were analyzed using the χ^2 test or Fischer's exact test (based on the samples) with OR and 95%CI. A p value of < 0.05 was considered as statistically significant.

Table 1 Demographics of patients included in the study. Values are given as n (%) or mean ± SD, as appropriate

	Control group ($n = 60$)	Treatment group ($n = 50$)	p
Males	32 (53.3%)	22 (44%)	0.3
Females	28 (46.6%)	28 (56%)	0.3
Age (years)	68.6 ± 6.2	68.5 ± 9.4	0.9
Weight (kg)	75.6 ± 14.5	73.1 ± 16.2	0.4
Height (cm)	164 ± 26.2	169 ± 19.8	0.3
BMI (kg/m^2)	27.5 ± 3.2	28.1 ± 4.1	0.4

Table 2 Comorbidities of the two treatment groups. No significant differences between groups in any comorbidity considered

	Control group ($n = 60$)	Treatment group ($n = 50$)	p
Hypertension	46 (76,6%)	44 (88%)	0.35
Diabetes	11(18%)	12(24%)	0.23
Coronaropathy	22 (36,6%)	19(38%)	1.00
Rheumatoides arthritis	6 (10%)	7(14%)	0.56
HCV	4 (6,6%)	3(6%)	1.00
Polivascular disease	4 (6,6%)	2(4%)	0.69
Antiplatelets therapy	24 (40%)	22(44%)	0.70

Results

Patient characteristics are reported in Table 1. No statistical differences were observed between the two groups for any variable. Comorbidities were also comparable between the two treatment groups (Table 2).

The rate of patients in the group treated with EVICEL® who received allogeneic RBC transfusions and/or plasma transfusion (28/50; 56%) was significantly reduced in comparison with patients in the control group (55/60; 91.7%) ($p < .0001$; OR: 0.098–95%CI: 0.029–0.314). Considering the single type of transfusion, the same results were observed for allogenic RBC transfusions (treatment group: 56%; control group: 91.7%; $p < 0.0001$; OR: 0.029–95%CI: 0.008–0.098) and plasma transfusions (treatment group: 38%; control group: 63.3%; $p = 0.02$; OR: 0.401–95%CI: 0.168–0.947) (Fig. 1).

Total RBC and plasma transfusion units transfused in the treatment group versus control group were 68 (42 RBC units and 26 plasma units) and 217 (146 RBC units and 71 plasma units) ($p < .0001$), respectively. Median number of RBC units transfused was significantly higher in the control group in comparison with the treatment group (3 [range 0–4] vs. 1 [range 0–2]; $p < .0001$), as well as the median number of plasma units transfused (2 [range 0–3] vs. 0 [range 0–2]; $p = .003$) (Table 3). These quantities corresponded to 0.84 RBC units and 0.52 plasma units per patient in the treatment group and to 2.43 RBC units, and 1.18 plasma units per patient in the control group (Table 3).

The volume of re-infused autologous blood was 345 ± 170 mL and 685 ± 338 mL in the treatment and control groups, respectively ($p < 0.0001$) (Table 3), thus showing a reduction in the early post-operative blood loss with the use of the fibrin sealant.

The median length of hospital stay per patient was significantly shorter for patient in the treatment group (7 [6–9] vs. 10 [9–13]; $p = 0.0001$) (Table 3).

The economic analysis compared the average resource consumed in the two groups for each patient. For quantification purposes, the following costs were used: 153 € for each RBC unit transfused, 161 € for each plasma unit transfused, and 500 € for each hospital day. These prices were obtained from the Financial Unit of our Hospital.

The economic analysis revealed higher costs per patients in the control group in comparison with the treatment group (control group: 5837.82 € vs. treatment group: 4256.08 €), taken also in consideration the cost of EVICEL® 5 mL for each patient in the treatment group, which was 452 €. This

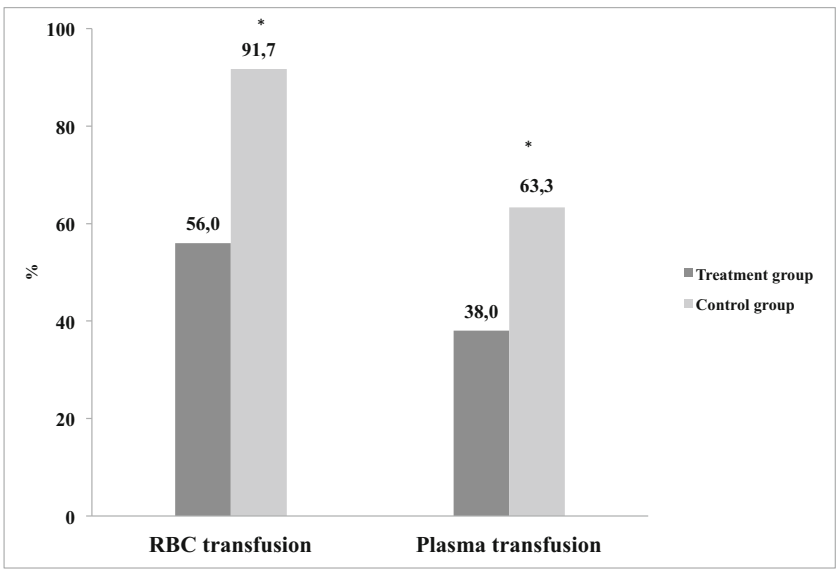

Fig. 1 Percentage of RBC and plasma transfusion after surgery in the two treatment groups. Asterisk means significant difference in favour of treatment group

Table 3 Clinical outcomes. Values are given as mean ± SD or median [range], as appropriate

	Treatment group ($n = 50$)	Control group ($n = 60$)	P value
Reinfused blood (mL)	345 (170)	685 (338)	< .0001
RBC transfused (units)	1 [0–2]	3 [0–4]	< .0001
RBC transfused/patient	0.84	2.43	< 0.001
Plasma transfused plasma (units)	2 [0–3]	0 [0–3]	0.003
Plasma transfused/patient	0.52	1.18	0.004
Hospital stay (days)	7 [6–9]	10 [9–13]	< 0.001

produced an average saving of 1581.64 € for each eligible patient (Fig. 2). Total and percent costs for each parameter in the two groups are reported in Table 4.

Considering that currently 1.160 patients per year are operated for total hip arthroplasty or in our Hospital, it may be calculated that 50 of them can be candidate for the use of blood management protocol with the use of EVICEL®. The budget impact analysis shows a potential cost saving of approx. 80,000 € per year and an average saving of more than 400,000 € over a period of five years (Fig. 3).

Discussion

This retrospective study demonstrated that the association of a fibrin sealant such as EVICEL® and a blood-saving protocol can reduce the need for RBC and plasma transfusion, hospital stay, and overall costs in patients undergoing complete RHA.

The results from this study seem to support the hypothesis that the use of a fibrin sealant may reduce total blood loss, as highlighted by the reduction of RBC, both allogenic and autologous, and plasma transfusions. With regard to adverse events and post -op. complication related to the use of EVICEL®, in literature, there have documented cases of surgical site infections and air embolism, due to the application of higher spraying pressure at a short distance from the target tissue; in our experience, respecting all the recommendations of the manufacturer, EVICEL® proved to be easy and safe to use, and the safety monitoring prior and after patients' discharge (including haematoma, infections, embolism, and DVT) did not reveal significant difference between the treatment and the control group.

The effect of fibrin sealants on blood loss during orthopedic procedure is still controversial. Indeed, several clinical studies have shown that the previous version of EVICEL®, fibrin sealant QUIXIL, significantly reduced blood loss in patients undergoing total hip or total knee replacement [18–21]. In contrast, another study evaluating blood loss and number of blood transfusions in patients undergoing total knee replacement (TKR) was not able to demonstrate any advantage in using the fibrin sealant [22]. In a study on 165 patients undergoing TKR, the authors concluded that the use of platelet gel and fibrin sealant improves the range of motion (ROM), reduces hospital stay, and may reduce the incidence of arthrofibrosis [23]. Finally, two other studies did not demonstrate that EVICEL® had a positive effect on blood loss, need for allogenic transfusion [24], in reducing drain output, or in facilitating early functional recovery after TKR [25].

All these studies were conducted on low-risk patients and most of the data refers to TKA. The patients included in this

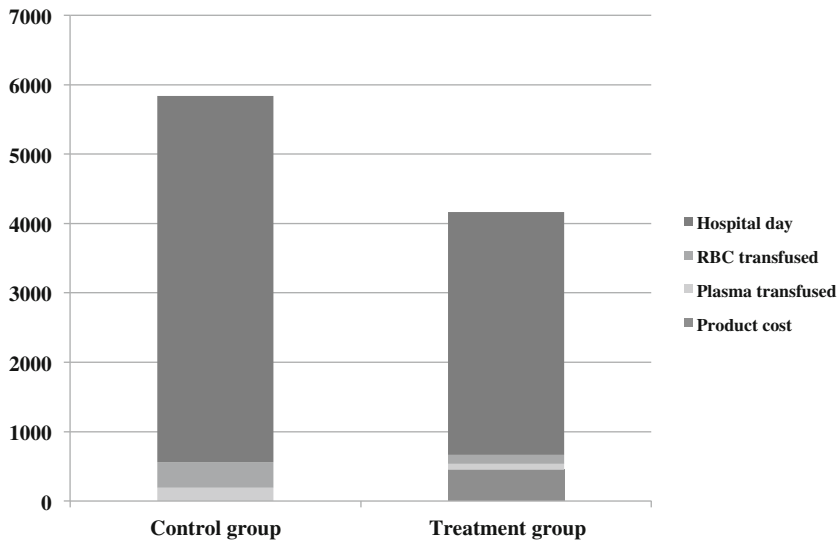

Fig. 2 Evaluation of the costs for a single patient treated in both groups. Significantly lower costs related to RBC/plasma transfusion and hospital stay were documented in the treatment group

Table 4 Breakdown of the average cost per patient by type of resource

	Treatment group ($n = 50$)	Control group ($n = 60$)
RBC transfused	128.52 € (3.09%)	372.30 € (6.38%)
Plasma transfused	83.72 € (2.01%)	190.52 € (3.26%)
Hospital day	3591.84 € (84.05%)	5275.00 € (90.36%)
Product cost	452.00 € (10.85%)	0 € (0%)

study underwent complete RHA, which implies a high risk of significant intra- and post-operative blood loss and requires the availability of blood and careful management of both the intra-operative and the post-operative phase. This surgery is often performed on ASA 3 patients who are often on anti-platelet agents or suffer from conditions altering coagulation. This type of patients was mostly excluded from other studies evaluating the effects of fibrin sealants on blood loss and transfusion rate. Moreover, in this study, we evaluated EVICEL® as an adjunct to a blood-saving protocol. To our knowledge, this setting was not previously evaluated. A recent study described the impact of the administration of tranexamic acid (TNA) within a blood-saving protocol [26], demonstrating that TNA reduced the allogenic transfusion rate in bilateral TKA, thus confirming that additional measures to a blood-saving protocol can bring further advantages and blood-saving effects. In out protocol, TNA was administered to both groups, so that the net effect on transfusion needs may be totally ascribed to the use of EVICEL®, which may have a different action in comparison with TNA. Indeed, EVICEL® is applied at the end of the surgery, so that post-operative blood loss is the only fraction that might be affected by its use and the adoption of all the possible techniques and resources aimed at reducing intra-operative blood loss for all patients deriving from the blood-saving protocol should allow to evaluate the net effect of the fibrin sealant. Based on the results of the present study, the use of fibrin sealant appears particularly indicated in subjects with lower Hb values in whom pre-op. pharmacological strategies were unsuccessful in increasing haemoglobin.

This study also demonstrated that, despite the higher costs related to the use of EVICEL®, the introduction of the fibrin sealant in the blood-saving protocol reduced total costs for the hospital. Limited data are available to evaluate cost-effectiveness of fibrin sealant in orthopaedic procedures. Two studies showed that fibrin sealants, and in particular EVICEL®, reduced overall costs. In particular, Colombo et al. [27] showed that fibrin sealant patch used in surgical procedures induced an average savings of about 304.00 € per patient. Moreover, Lim et al. [28] demonstrated that the use of EVICEL® for dural closure may result in important cost savings for hospitals (around 200.00 € per patient), partly driven by the reduced need for other adjunctive and rescue therapies. These data are in accordance with the findings of the present study, which show an even higher cost reduction related to the use of EVICEL® within a blood-saving protocol. This may be due to the fact that the patients included in the study were high-risk patients, with severe comorbidities, high anaesthesiologic risks and undergoing a procedure potentially exposing to a relevant blood loss. The use of a method to significantly reduce the need for post-operative transfusion (possibly due to the reduction of post-operative blood loss) may have a significant impact on hospital stay and further treatments and, thus, on costs. The significant reduction in hospital stay also allows a higher patients turnover, which also allows the treatment of a higher number of patients and, thus, an additional advantage for the hospital.

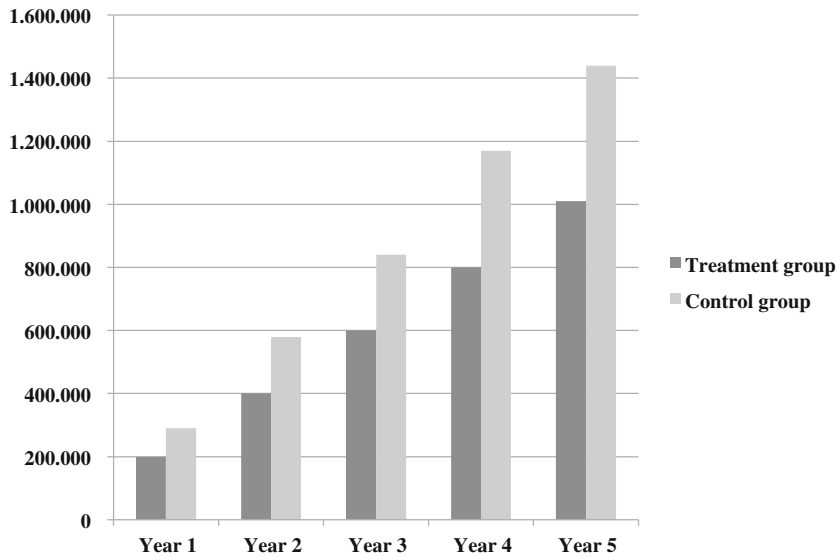

Fig. 3 Estimation of potential money savings (in Euro) over a 5-year period (considering 50 patients per year eligible for EVICEL treatment)

This study has some limitations, the first being its retrospective design. All efforts were done to set strict inclusion and exclusion criteria for the selection of the patients and this is reflected by the lack of significant differences in baseline variables between the two groups. The two groups of patients were operated on and evaluated during two different time periods, adding to the risk of potential bias. Anyway, all surgeries were performed by the same surgical team, including the same anaesthesiologist, following the same, standardized protocol for both groups, without any difference in any aspect of patient management. These measures should have limited the risk of bias. Furthermore, the retrospective collection of data is also a limiting factor for cost assessment and reporting, and therefore the apparent huge advantage related to the use of EVICEL® should be demonstrated in the setting of a comparative prospective trial, and hypothetical money saving should be confirmed by real-world calculations.

Another flaw of the present trial is the limited number of patients. On the other hand, power analysis showed acceptable power of the study, which may be used as a reference for future to plan larger randomized controlled trials to confirm the results of the present study.

Conclusion

This study suggests that the adoption of a blood-saving protocol with the inclusion of a fibrin sealant may significantly reduce post-operative blood transfusions and induce a faster recovery for patients undergoing complete RHA, allowing early discharge from the hospital. These advantages seem to provide significant cost savings for both the hospital and the healthcare system. Further trials, with a randomized design, are needed to confirm the findings of the present study.

Compliance with ethical standards

The study protocol was notified to Humanitas Research Hospital (ICH) Ethical Committee. During the study, the data were collected in complete anonymity and handled according to the local law on privacy. The ICH blood management protocol is compliant with the Declaration of Helsinki, to standards EN ISO 14155:1, EN ISO 14155:2 and Good Clinical Practices (GCP). Moreover, all personnel involved in the study agreed to act in accordance with the principles contained in these GCPs.

Disclosure statement All the authors of the present manuscript have nothing to disclose.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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References

1. Bierbaum BE, Callaghan JJ, Galante O, Rubash HE, Tooms RE, Welch RB (1999) An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 81:2–10
2. Bong MR, Patel V, Chang E, Issack PS, Hebert R, Di Cesare PE (2004) Risks associated with blood trasfusion after total knee arthroplasty. J Arthroplast 19:281–287. https://doi.org/10.1016/j.arth.2003.10.013
3. Sehat K, Evans R, Newman J (2000) How much blood is really lost in total knee arthroplastic? Correct blood loss management should take hidden loss into account. Knee 7:151–155. https://doi.org/10.1016/S0968-0160(00)00047-8
4. Spahn DR (2010) Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 113:482–495. https://doi.org/10.1097/ALN.0b013e3181e08e97
5. Husted H, Holm G, Jacobsen S (2008) Predictor of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. Acta Orthop 79:168–173. https://doi.org/10.1080/17453670710014941
6. Lemaire R (2008) Strategies for blood management in orthopaedic and trauma surgery. J Bone Joint Surg (Br) 90:1128–1136. https://doi.org/10.1302/0301-620X.90B9.21115
7. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, Khreiss M, Dahdaleh FS, Khavandi K, Sfeir PM, Soweid A, Hoballah JJ, Taher AT, Jamali FR (2011) Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. Lancet 378:1369–1407. https://doi.org/10.1016/S0140-6736(11)61381-0
8. Borghi B, Casati A (2000) Incidence and risk factors for allogenic blood transfusion during major joint replacement using an integrated autotransfusion regimen. The Rizzoli Study Group on Orthopaedic Anaesthesia. Eur J Anaesthesiol 17:411–417. https://doi.org/10.1097/00003643-200007000-00002
9. Villatte G, Engels E, Erivan R, Mulliez A, Caumon N, Boisgard S, Descamps S (2016) Effect of local anaesthetic wound infiltration on acute pain and bleeding after primary total hip arthroplasty: the EDIPO randomised controlled study. Int Orthop 40(11):2255–2260. https://doi.org/10.1007/s00264-016-3133-3
10. Reina N, Fennema P, Hourlier H (2017) The impact of mild perioperative hypothermia on the effectiveness of tranexamic acid in total hip arthroplasty. Int Orthop 41(1):55–60. https://doi.org/10.1007/s00264-016-3170-y
11. Sucher MG, Giordani M, Figoni A, Nedopil AJ (2016) Perioperative blood-loss after total hip arthroplasty can be significantly reduced with topical application of epsilon-aminocaproic acid. Int Orthop 40(10):2019–2023. https://doi.org/10.1007/s00264-015-3103-1
12. Green AL, Arnaud A, Batiller J, Eljamel S, Gauld J, Jones P, Martin D, Mehdorn M, Ohman J, Weyns F (2014) A multicentre, prospective, randomized, controlled study to evaluate the use of a fibrin sealant as an adjunct to sutured dural repair. Br J Neurosurg 12:1–7. https://doi.org/10.3109/02688697.2014.948808
13. Bou Monsef J, Buckup J, Waldstein W, Cornell C, Boettner F (2014) Fibrin sealants or cell saver eliminate the need for autologous blood donation in anemic patients undergoing primary total knee arthroplasty. Arch Orthop Trauma Surg 134:53–58. https://doi.org/10.1007/s00402-013-1876-5
14. Padgett D, Lewallen D, Penenberg B, Hanssen A, Garvin K, Mahoney O, Kinsey T (2009) Surgical technique for revision Total hip replacement. J Bone Joint Surg Am 91(Suppl 5):23–28. https://doi.org/10.2106/JBJS.I.00363

15. Greenky M, Shaner J, Rasouli MR, Han SB, Parvizi J, Hozack WJ (2014) Intraoperative blood salvage in revision total hip arthroplasty: who benefits most? J Arthroplast 29(6):1298–1300. https://doi.org/10.1016/j.arth.2013.12.009
16. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, Colwell CW, American College of Chest Physicians (2008) Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). Chest 133(Suppl 6):381S–453S. https://doi.org/10.1378/chest.08-0656
17. Nicolaides AN, Fareed J, Kakkar AK, Breddin HK, Goldhaber SZ, Hull R, Kakkar VV, Michiels JJ, Myers K, Samama M, Sasahara A, Kalodiki E (2006) Prevention and treatment of venous thromboembolism. International consensus statement (guidelines according to scientific evidence). Int Angiol 25:101–161. https://doi.org/10.1177/1076029612474840
18. Levy O, Martinowitz U, Oran A, Tauber C, Horoszowski H (1999) The use of fibrin tissue adhesive to reduce blood loss and the need for blood transfusion after total knee arthroplasty. J Bone Joint Surg 81:1580–1588
19. Wang GJ, Hungerford DS, Savory CG, Rosenberg AG, Mont MA, Burks SG et al (2001) Use of fibrin sealant to reduce bloody drainage and hemoglobin loss after total knee arthroplasty: a brief note on a randomized prospective trial. J Bone Joint Surg Am 83:1503–1505
20. Wang GJ, Goldthwaite CA Jr, Burks S, Crawford R, Spotnitz WD, Orthopaedic Investigators Group (2003) Fibrin sealant reduces perioperative blood loss in total hip replacement. J Long Term Eff Med Implants 13:399–411. https://doi.org/10.1615/JLongTermEffMedImplants.v13.i5.50
21. Crawford RW, Giangrande P, Murray D (1999) Fibrin sealant reduces blood loss in total hip arthroplasty. Hip Int 9:127–132. https://doi.org/10.1177/112070009900900302
22. Kluba T, Fiedler K, Kunze B, Ipach I, Suckel A (2012) Fibrin sealants in orthopaedic surgery: practical experiences derived from use of QUIXIL® in total knee arthroplasty. Arch Orthop Trauma Surg 132:1147–1152. https://doi.org/10.1007/s00402-012-1519-2
23. Everts PAM, Devilee RJ, Oosterbos CJ, Mahoney CB, Schattenkerk ME, Knape JT et al (2007) Autologous platelet gel and fibrin sealant enhance the efficacy of total knee arthroplasty: improved ROM, decreased length of stay and a reduced incidence of arthrofibrosis. Knee Surg Sports Traumatol Arthrosc 15:888–894. https://doi.org/10.1007/s00167-007-0296-x
24. Randelli F, D'Anchise R, Ragone V, Serrao L, Cabitza P, Randelli P (2014) Is the newest fibrin sealant an effective strategy to reduce blood loss after total knee arthroplasty? A randomized controlled study. J Arthroplast 29:1516–1520. https://doi.org/10.1016/j.arth.2014.02.024
25. Skovgaard C, Holm B, Troelsen A, Lunn TH, Gaarn-Larsen L, Kehlet H, Husted H (2013) No effect of fibrin sealant on drain output or functional recovery following simultaneous bilateral total knee arthroplasty: a randomized, double-blind, placebo-controlled study. Acta Orthop 84:153–158. https://doi.org/10.3109/17453674.2013.769082
26. Kim TK, Chang CB, Kang YG, Seo ES, Lee JH, Yun JH, Lee SH (2014) Clinical value of tranexamic acid in unilateral and simultaneous bilateral TKAs under a contemporary blood-saving protocol: a randomized controlled trial. Knee Surg Sports Traumatol Arthrosc 222:1870–1878. https://doi.org/10.1007/s00167-013-2492-1
27. Colombo GL, Caruggi M, Ottolini C, Di Matteo S, Valentino MC, Bruno GM (2015) Economic evaluation of fibrin sealant patch: a proposal to assess the economic value in hemostasis and as a surgical sealant. Value Health 18:A533. https://doi.org/10.1016/j.jval.2015.09.1665
28. Lim S, Ferko N, Tibensky B, Danker WI, Jamous N, Batiller J, Kocharian R (2015) Economic analysis of Evicel® compared with standard of care for Dural closure in elective cranial surgery: a United Kingdom hospital perspective. Value Health 18:A369. https://doi.org/10.1016/j.jval.2015.09.742