SYSTEMATIC REVISION AND META-ANALYSIS OF HEMOSTATIC MATRICES FOR BLEEDING CONTROL

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INTRODUCTION

It is estimated that bleeding complications occur in approximately 30% of surgeries. (Echave, 2014) Excessive, uncontrolled surgical bleeding might lead to patient morbidity and mortality, as well as an increase in intra- and post-operative complications and hospital resource utilization, such as blood transfusions and additional length of stay, imposing a heavy clinical and economic burden. Thus, achieving hemostasis is critical to prevent the former complications and events, which might yield potential clinical and economic benefits for patients, surgeons, hospitals and payers.

Hemostatic matrices with human thrombin (Surgiflo™ & Floseal™) are well-known safe and effective products indicated as adjuncts to achieve hemostasis in surgical procedures, particularly when conventional techniques (sutures, cautery or ligature) are ineffective or impractical, or in situations where other hemostatic agents are not indicated due to the risk of damaging vital structures. Absorbable porcine (Surgiflo™) and bovine (Floseal™) gelatin matrices with thrombin have individually shown to be safe and effective hemostats in cardiovascular (CV), neuro-spine (SP) and urinary tract (UT) procedures. However, comparative safety and efficacy outcomes would result of the interest of multiple stakeholders for decision making.

OBJECTIVE

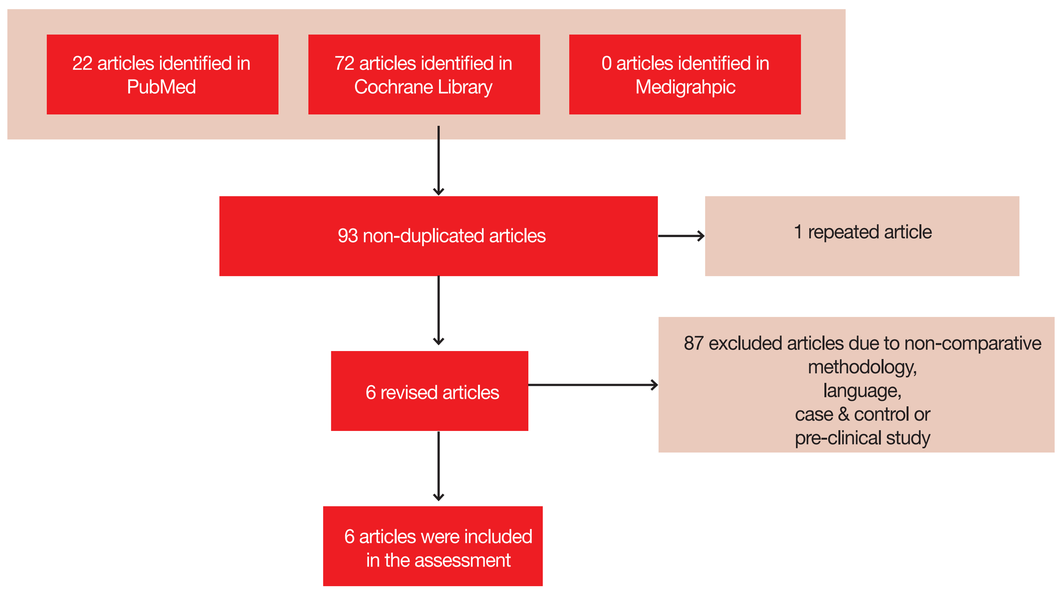
The objective of the present study was to evaluate Surgiflo™'s a nd F loseal™'s comparative safety and effectiveness, as well as additional outcomes, in CV, SP and UT procedures by performing a systematic review and meta-analysis of published literature.

METHODS

A systematic search of current published literature on safety and effectiveness of hemostatic matrices was performed to identify studies or trials where a direct comparison between the porcine and bovine gelatin matrices would have taken place. Used methodology focused on the combined use of the following MeSH terms surgical hemostasis, and the following key words: gelatin thrombin hemostatic matrix, floseal, surgiflo, surgical hemostasis meta-analysis, clinical trials & reviews. PubMed, The Cochrane Library y MediGraphic were the searched databases to perform the search. Additional filters were used to guarantee the words Floseal™ & Surgiflo™ would appear either on the title or in the abstract. Inclusion criteria included publications in English and Spanish up to December 2015, randomized controlled trials (RCTs) or retrospective analyses.

A total of 94 relevant studies were found; from them all, a duplicate was found in any of the other searched databases. Afterwards, only those publications where both hemostatic matrices were compared were selected; additional exclusion criteria included case & control studies and pre-clinical data. At the end, 87 articles were excluded, and the remaining 7 were subject to a deeper revision; 6 publications met all inclusion criteria (39,660 patients). Figure 1 shows the diagram for the systematic literature revision.

Figure 1. Flow diagram, systematic revision of evidence.



Source: own ellaboration

All of the final studies were assessed, along with all shown variables & potential comparison basis between them. Thus, 6 indicators were identified for posterior comparison, with at least 2 studies providing data for each of the former (Table 1).

Table 1. Assessed comparisons

Indicator	Included studies
Blood transfusions	(Nogueira, Katz, Pinochet, Kurta, & Coleman, 2008), (Tackett, Calcaterra, Magee, & Lattouf, 2014), (David, Lim, Gunnarsson, Kocharian, & Roy, 2015), (Price, Tackett, & Patel, 2015)
Surgical / OR time	(Tackett, Calcaterra, Magee, & Lattouf, 2014), (David, Lim, Gunnarsson, Kocharian, & Roy, 2015), (Price, Tackett, & Patel, 2015)
Length of hospital stay	(Tackett, Calcaterra, Magee, & Lattouf, 2014), (Price, Tackett, & Patel, 2015)
Major complications	(Nogueira, Katz, Pinochet, Kurta, & Coleman, 2008) , (Tackett, Calcaterra, Magee, & Lattouf, 2014), (Price, Tackett, & Patel, 2015)
Minor complications	(Nogueira, Katz, Pinochet, Kurta, & Coleman, 2008) , (Tackett, Calcaterra, Magee, & Lattouf, 2014), (Price, Tackett, & Patel, 2015)
Hemostasis in < 7 minutes	(Landi, Gregori, Marotta, & Delfini, 2015), (Gazzeri, Galarza, & Alfier, 2012)

RESULTS

Once comparable data were pooled from the articles, they were meta-analyzed using specialized software RevMan v.5.3. Two types of analyses were performed, depending on available information from the clinical trials. For those comparisons where means and standard deviations were used, cohort mean differences were assessed. Similarly, odds ratios (ORs) were used for those comparisons reporting the incidence/number of events, as literature suggests. (Deeks, 1998).

To address heterogeneity, this analysis considered random effects models while using the I^2 statistic, as it allows to incorporate the former within the meta-analysis. Figures 2-7 show the Forest Plots for all considered indicators. All Forest Plots show **no statistically-significant differences between the porcine and bovine hemostatic matrices for any of the considered indicators**. Table 2 summarizes estimated ORs and mean differences (95% confidence intervals). Substantial (>50%) and small (<25%) heterogeneity was observed.

Figure 2. Forest Plot – blood transfusions

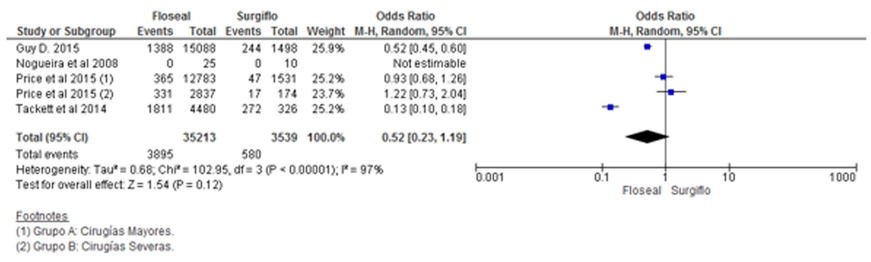


Figure 3. Forest Plot – surgical / OR time

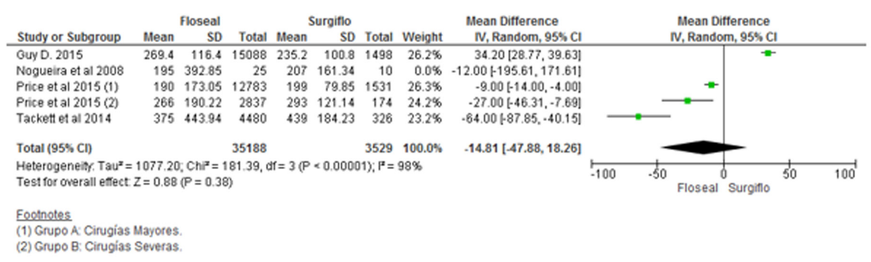


Figure 4. Forest Plot – length of hospital stay

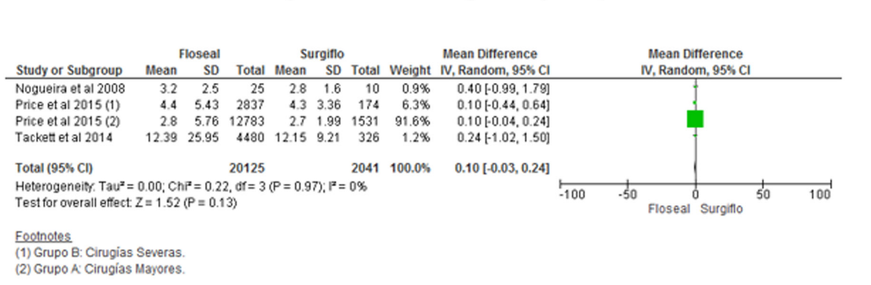


Figure 5. Forest Plot – major complications

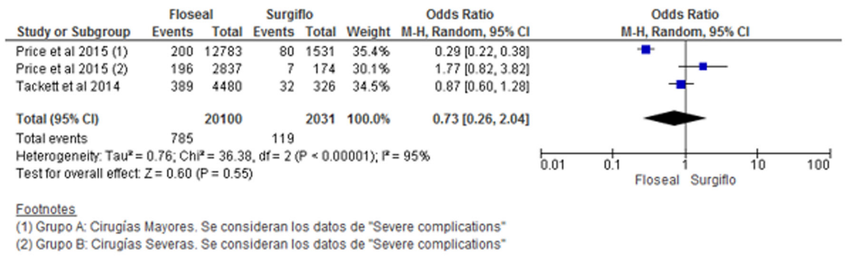


Figure 6. Forest Plot – minor complications

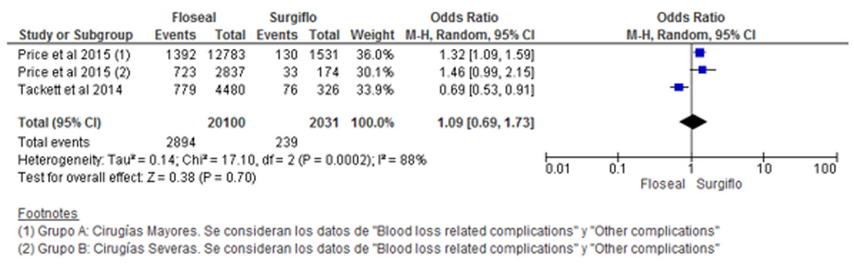


Figure 7. Forest Plot – hemostasis in < 7 minutes

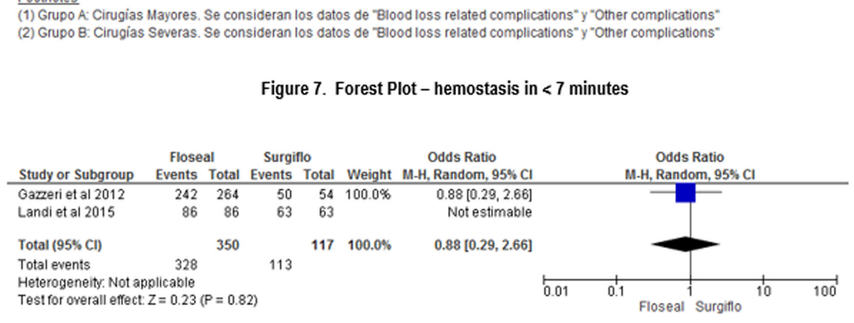


Table 2. Comparison results

Indicator	Results, ORs M-H, Random. (95% CI)
Blood transfusions	0.52 (0.23, 1.19)
Surgical / OR time	-14.81 (-47.88, 18.26)*
Length of hospital stay	0.10 (-0.03, 0.24)*
Major complications	0.73 (0.26, 2.04)
Minor complications	1.09 (0.69, 1.73)
Hemostasis in < 7 minutes	0.88 (0.29, 2.66)

**In these comparisons, outcomes were analyzed through mean differences.*

CONCLUSIONS

This systematic review & meta-analysis of published literature shows there are no statistically-significant differences between the considered hemostatic matrices for the listed indicators. Both products have components, indications and application methods that yield similar safety and efficacy outcomes for the considered procedures. Both technologies could be used indistinctly for the considered surgical specialties, with product choice having no impact on clinical outcomes.

REFERENCES

1. David, G., Lim, S., Gunnarsson, C., Kocharian, R., & Roy, S. (2015). Similar patient outcomes yet different hospital costs between flowable hemostatic agents. Journal of medical economics, 735-745.
2. Deeks, J. (1998). Odds ratios should be used only in case-control studies and logistic regression analyses. BMJ, 317-1155.
3. Echave, M. (2014). Use of Floseal, a human gelatine-thrombin matrix sealant, in surgery: a systematic review. BMC Surgery.
4. Gazzeri, R., Galarza, M., & Alfier, A. (2012). Safety biocompatibility of gelatin hemostatic matrix (Floseal and Surgiflo) in neurosurgical procedures. . Surgical technology international, 49-54.
5. Higgins, J., & Green, S. (2011). Cochrane Handbook for Systematic Reviews of Interventions. Obtenido de http://handbook.cochrane.org/
6. Landi, A., Gregori, F., Marotta, N., & Delfini, R. (2015). Efficacy, security, and manageability of gelified hemostatic matrix in bleeding control during thoracic and lumbar spine surgery: FloSeal versus surgiflo. 7. Journal of Neurological Surgery Part A: Central European Neurosurgery.
8. Nogueira, L., Katz, D., Pinochet, R., Kurta, J. M., & Coleman, J. A. (2008). Comparison of gelatine matrix- thrombin sealants used during laparoscopic partial nephrectomy. BJU international, 1670-1674.
9. Price, J. S., Tackett, S., & Patel, V. (2015). Observational evaluation of outcomes and resource utilization from hemostatic matrices in spine surgery. Journal of medical economics, 18(10), 777-786.
10. Tackett, S. M., Calcaterra, D., Magee, G., & Lattouf, O. M. (2014). Real-world outcomes of hemostatic matrices in cardiac surgery. Journal of cardiothoracic and vascular anesthesia, 28(6), 1558-1565.

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