Research Article

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Using flowable gelatin in anterior cervical spine surgery in real-world practice: a retrospective cohort study

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Aim: To assess the clinical and economic impact of flowable gelatin hemostatic matrix (FGHM) in anterior cervical spine surgery (ACSS). **Patients & methods:** A total of 451 patients with performed ACSS were included to compare FGHM with conventional hemostatic methods for clinical and cost outcomes using propensity score matching method. **Results:** The comparisons of the matched 125 pairs observed that FGHM was associated with significantly lower blood transfusion volume (11.2 vs 36.3 ml; p = 0.039), shorter postsurgery hospital stay length (3.7 vs 4.7 days; p = 0.002), shorter operation time (103.5 vs 117.7 min; p = 0.004), lower drainage placement rate (51.2 vs 89.6%; p < 0.001) and also lower total hospital costs (median ¥64,717 vs ¥65,064; p = 0.035). **Conclusion:** Use of FGHM in ACSS improved perioperative outcomes without increasing hospital costs.

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Keywords: anterior cervical spine surgery • flowable gelatin hemostatic matrix • hemostasis • hospital costs • propensity scored matching

Anterior approach is the most common cervical spine surgery technique [1]. One of the difficulties during anterior cervical spine surgery (ACSS) is to stop the epidural venous oozing. If hemostasis is not achieved promptly, the reduced surgical visual field could result in higher risk of iatrogenic injury on nerve and longer operation time [2]. Also, studies have demonstrated that massive blood loss is associated with mortality and utilizing more health resource [3,4]. Therefore, many hemostatic measures have been implemented to control bleeding of epidural venous plexus. Adjunctive absorbable hemostatic agents, such as oxidized regenerated cellulose, gelatin sponge and collagen sponge have been used in ACSS for many years [4–6]. However, these products are difficult to position in the deep, narrow and suboptimally visualized bleeding sites during ACSS procedures [7].

The absorbable and flowable gelatin hemostatic matrix (FGHM) SURGIFLO® was approved by the China Food and Drug Administration in 2011. It stops bleeding by accelerating blood clot formation with the gelatin matrix and is able to reach difficult-to-access bleeding sites due to its flowable property. Many studies [8–10] have investigated the efficacy on hemostasis in various surgeries using FGHM preloaded with thrombin, including few clinical reports regarding the use of FGHM in spinal surgery [11,12]. A randomized clinical trial showed that the hemostasis efficacy of flowable gelatin matrix in posterior spinal fusion for idiopathic scoliosis decreased intraoperative blood loss by 30% [11]. A multicenter prospective clinical trial demonstrated that the efficacy of flowable gelatin matrix (Proceed) on hemostasis for different bleeding sites during spine surgery [12]. However, the literature lacks research on FGHM in ACSS and regarding related economic outcomes. Additionally, the real-world evidence clarifying the hemostatic effects of FGHM in Chinese patients with ACSS was lacking and using health economic evidence from western countries to support reimbursement decision making in China has become challengeable. Thus, we conducted

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this study to assess the impact of FGHM hemostatic matrix (SURGIFLO) in ACSS on the perioperative clinical outcomes associated with hemostasis and direct hospital costs in a Chinese tertiary hospital.

Patients & methods

This was a retrospective study including patients who underwent ACSS for cervical degenerative disease at a single institution from January 2014 to December 2016. The research proposal of this study was reviewed and approved by the research ethics board in the study institution.

Data source & extraction

The medical and billing records were exported from the hospital electronic database. The hospital database contains information on patient demographics, socioeconomic status, first and final diagnosis as well as comorbidities. The laboratory test records were used for screening patient's baseline of coagulation function one day before operation. The surgical records provided information on operation time, type of procedure, operation site, volume of blood loss as well as autologous and allogeneic blood transfusion during surgery. The medical notes included records of operation-related complications. The postoperative length of stay (LOS) was calculated as the date difference between surgery and discharge. The exported billing records were summed to provide total direct cost. To allow further analysis, all charge details were clustered into 15 cost categories: topical absorbable hemostatic (TAH) agent, implanted devices for fixation, medicine, disposable supplies, blood transfusion, hospital bed, medical image, laboratory tests, anesthesia, operation, other therapy, nursing service, personal care, in-hospital dining and others.

Patient selection

Generally, FGHM is applied to the bleeding that cannot be adequately controlled by traditional hemostatic agents, which leads to the higher risk of bleeding associated with utilization of FGHM. This clinical practice could confound the hemostatic effects of FGHM compared with traditional hemostatic agents after the introduction of FGHM (January 2015). Thus, this study included patients who underwent ACSS in 2014 to create the historical control group (HC), whereas the FGHM group was created by including patients who underwent ACSS with the utilization of FGHM in 2015 and 2016. This study identified patients using the following two inclusion criteria: operation position was between C2 and C6; operation procedure was anterior cervical corpectomy with fusion or anterior cervical discectomy with fusion. Additionally, this study used the following exclusion criteria to control potential bias: applied thrombin prior to or during operation; history of spinal surgery; operation for nondegenerative diseases, such as trauma, tumor, or infection; other irrelevant operations during the same hospital episode for ACSS; multiple surgical sites unrelated to ACSS; insufficient information for analysis.

Statistical analysis

Individuals usually differ in various baseline characteristics, such as type of procedures and number of fusion cages, which could directly affect postoperative outcomes, resulting in biased estimation on effect. To manage this bias, propensity score matching was applied. The confounders were identified by the unadjusted baseline comparison between groups using Student's t-test (for continuous variables) and Fisher exact test (for categorical variables). The 1:1 matched groups for FGHM versus HC were created by using greedy approach with criteria of propensity score difference less than 0.001. After the matching, all nonmatched cases from the database were discarded and the matched cases were used for further statistical analysis.

The matched groups were compared with the surgical outcomes and distribution of hospital costs using a paired *t*-test for continuous outcomes, McNemar test for dichotomous outcomes and Wilcoxon signed rank test for the distribution of hospital costs. Additionally, conventional regression analyses with adjustment for patient baseline characteristics were conducted to confirm the adjusted comparisons of measured outcomes related to blood transfusion and hospital costs. These regression analyses included logistic regression analysis for risk of blood transfusion, linear regression analysis for blood transfusion volume and generalized linear regression for hospital costs. Statistical software SAS 9.2 was used to conduct the data analysis described above and the statistical significance was defined as the two-sided p-value less than 0.05.

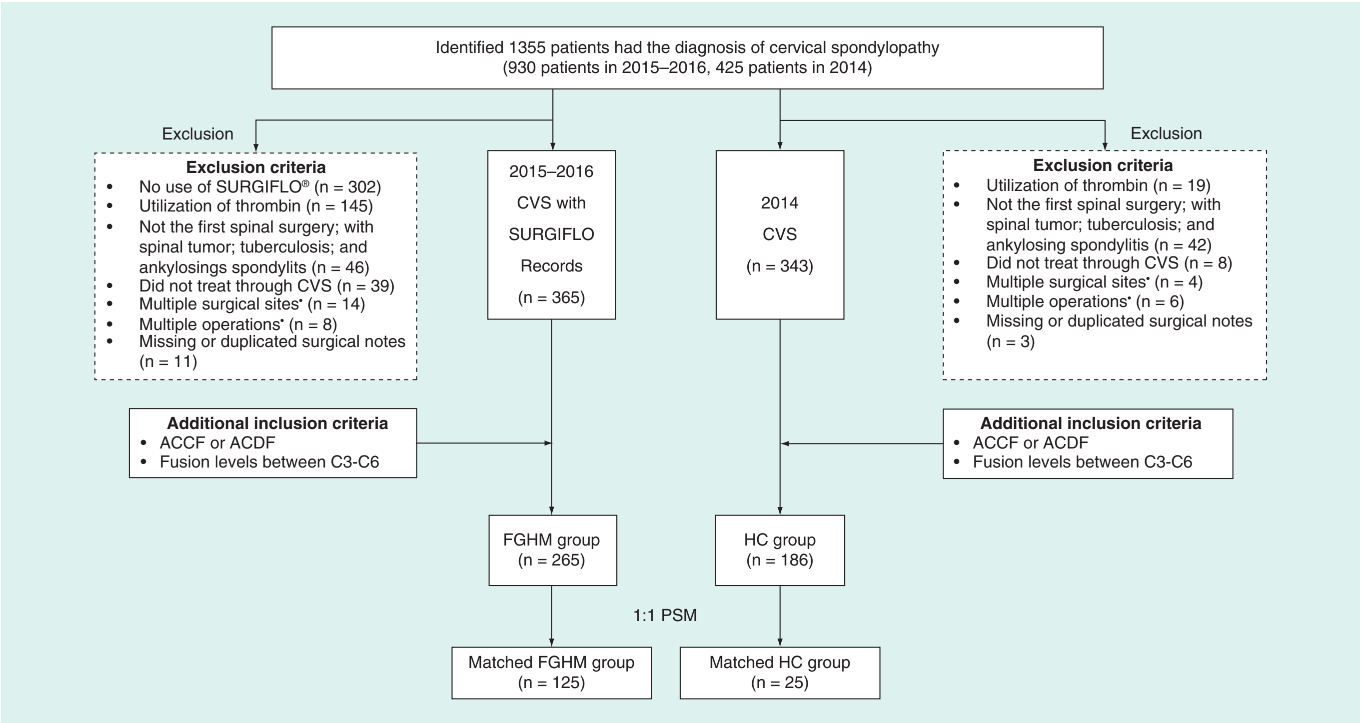

Figure 1. The patient flow of the study.
*Not for complication treatment.
ACCF: Anterior cervical corpectomy fusion; ACDF: Anterior cervical discectomy fusion; CVS: Cervical vertebrae surgery; FGHM: Flowable gelatin hemostatic matrix; HC: Historical control; PSM: Propensity score matching.

Results

The hospital (ward II and III, Department of Orthopedics) identified 425 patients in 2014 and 930 patients in 2015 and 2016, who had the diagnosis of cervical spondylopathy and were treated by surgery. According to the inclusion and exclusion criteria, 186 patients were included in the HC group and 265 patients were included in the FGHM group. The details of patient inclusion and exclusion are illustrated in Figure 1.

Baseline comparison before propensity score matching

The patient baseline characteristics associated with FGHM and HC before and after propensity score matching are summarized in Table 1. The direct comparisons of patient baseline characteristics of two created groups (FGHM vs HC) observed significant differences in the distributions of gender (male: 59.2 vs 72.0%; $p = 0.005$), employment status (full-time employment: 27.9 vs 54.3%; $p < 0.001$; unemployed: 35.1 vs 14.0%; $p < 0.001$), normal international normalized ratio (93.5 vs 97.8%; $p = 0.040$) and the distribution of surgery procedures (ACCF: 15.8 vs 31.2%; $p < 0.001$; anterior cervical discectomy with fusion: 84.2 vs 68.8%; $p < 0.001$). Additionally, the two groups were different in the distribution of the utilization of fusion cages (two cages: 42.6 vs 27.4%; $p = 0.001$; more than two cages: 9.1 vs 2.7%; $p = 0.006$) and titanium mesh (1.5 vs 14.5%; $p < 0.001$). These characteristics were included to develop propensity score calculation formula and then to identify 125 propensity score-matched pairs with well-balanced patient baseline characteristics for FGHM versus HC.

Adjusted comparisons of FGHM versus HC for perioperative outcomes

All matched patients used gelatin sponges for hemostasis during operation. However, the utilization of gelatin sponges was significantly less in matched FGHM patients (3.0 ± 1.3 vs 4.0 ± 1.1 bags; $p < 0.001$). The average use of FGHM in the matched patients was 1.0 unit (SD 0.1). The comparisons of the measured outcomes for matched FGHM versus matched HC observed lower blood transfusion volume (11.2 ± 62.5 vs 36.3 ± 115.4 ml; $p = 0.039$), shorter operation time (103.5 ± 35.0 vs 117.7 ± 39.6 min; $p = 0.002$), shorter postsurgery LOS (3.7 ± 1.9 vs 4.7 ± 3.1 days; $p = 0.004$), and lower rate of drainage tube placement (51.2 vs 89.6%; $p < 0.001$),

Table 1. Baseline before and after propensity score matching.

Variable	Mean ± SD/%		p-value	Mean ± SD/%		p-value
	FGHM group (n = 265)	HC group (n = 186)		Matched FGHM group (n = 125)	Matched HC group (n = 125)	
Patient characteristics						
Gender (males)	59.2	72	0.005	67.2	67.2	1.000
Age (years)	52.9 ± 10.0	52.1 ± 10.1	0.384	52.0 ± 9.5	51.3 ± 10.3	0.594
BMI (kg/m^2)	25.3 ± 3.6	26.6 ± 10.7	0.087	25.7 ± 3.9	26.9 ± 12.8	0.273
Full-time employment	27.9	54.3	<0.001	47.2	45.6	0.480
Unemployed	35.1	14.0	<0.001	23.2	17.6	0.296
Local public health insurance	17.4	14.0	0.363	12.8	12.8	1.000
Out-of-pocket costs for medical expenses	81.9	84.9	0.444	86.4	86.4	1.000
Drinking	9.1	11.3	0.524	10.4	12.8	0.700
Smoking	23.0	26.9	0.375	23.2	24.8	0.877
Normal INR	93.5	97.8	0.040	98.4	98.4	1.000
Normal hemoglobin	86.8	90.0	0.231	84.0	92.0	0.089
Normal erythrocytes	96.2	98.4	0.255	94.4	98.4	0.182
Cardiovascular comorbidity	11.7	17.7	0.076	11.2	17.6	0.230
Cerebral infarction comorbidity	1.1	3.8	0.100	0.0	5.6	0.265
Previous antiplatelet/coagulants agents	1.9	1.6	1.000	2.4	0.8	0.617
Treatment						
ACCF	15.8	31.2	<0.001	16.8	17.6	1.000
ACDF	84.2	68.8	<0.001	83.2	82.4	1.000
Number of operated vertebral levels	2.8 ± 0.7	2.7 ± 0.7	0.372	2.7 ± 0.7	2.7 ± 0.7	0.914
C4/C5	5.7	5.9	1.000	7.2	8.8	0.823
C5/C6	24.5	28	0.446	31.2	26.4	0.417
C6/C7	6.8	7.5	0.853	7.2	10.4	0.502
C3/C4/C5	4.2	6.5	0.285	4.0	4.8	1.000
C4/C5/C6	26.0	21.5	0.315	22.4	20.0	0.728
C5/C6/C7	16.2	16.1	1.000	16.0	17.6	0.850
C3/C4/C5/C6	8.3	4.8	0.187	6.4	4.8	0.773
C4/C5/C6/C7	7.5	8.6	0.726	4.8	5.6	1.000
C3/C4/C5/C6/C7	0.8	1.1	1.000	0.8	1.6	1.000
Number of cages = 0	0.4	12.9	<0.001	0.0	3.2	0.502
Number of cages = 1	47.9	57.0	0.069	59.2	57.6	0.803
Number of cages = 2	42.6	27.4	0.001	36.8	36.0	1.000
Number of cages >2	9.1	2.7	0.006	4.0	3.2	1.000
Number of implanted cages	1.6 ± 0.7	1.2 ± 0.7	<0.001	1.4 ± 0.6	1.4 ± 0.6	0.145
Utilization of titanium mesh	1.5	14.5	<0.001	2.4	2.4	1.000

ACCF: Anterior cervical corpectomy fusion; ACDF: Anterior cervical discectomy fusion; BMI: Body mass index; FG: Flowable gelatin; HC: Historical control; INR: International normalized ratio; SD: Standard deviation.

slight but nonsignificant decrease in intraoperative transfusion risk (3.2 vs 9.6%; p = 0.080). The results of the comparisons of surgical outcomes are summarized in Table 2. Multiple regression analysis with the adjustment for surgery procedure (anterior cervical corpectomy with fusion), operation site (C5 + C6), comorbidities and utilization of titanium mesh observed statistical significance for lower intraoperative blood transfusion risk (odds ratio 0.428; p = 0.032) but not for lower intraoperative blood transfusion volume (coefficient -18.319; p = 0.137) in patients with the utilization of FGHM (Figure 2).

Adjusted comparisons of the distribution of hospital costs for matched groups

The allocation of costs for two matched groups is summarized in Table 3. The utilization of FGHM significantly increased the costs of TAH agents (median ¥3105 vs ¥60; p < 0.001; average currency exchange during 2014 to 2016: US$1=¥6.3378) for the matched patients. However, in the matched FGHM group, significantly lower other

Table 2. Comparison of surgical outcomes in matched groups.

Variable	Mean ± SD/%		p-value
	Matched FGHM group (n = 125)	Matched HC group (n = 125)	
TAH agents			
SURGIFLO (units)	1.0 ± 0.1	–	
Gelatin sponges (bags)	3.0 ± 1.3	4.0 ± 1.1	<0.001
Operation time (min)	103.5 ± 35.0	117.7 ± 39.6	0.002
Hospital stay length (days)	6.9 ± 2.6	9.0 ± 3.7	<0.001
Postoperative LOS (days)	3.7 ± 1.9	4.7 ± 3.1	0.004
Intraoperative blood loss and transfusion			
Blood loss (ml)	61.0 ± 59.9	71.6 ± 55.2	0.157
Blood transfusion rate	3.2	9.6	0.080
Blood transfusion volume (ml)	11.2 ± 62.5	36.3 ± 115.4	0.039
Drain output			
Drainage tube placement rate	51.2	89.6	<0.001
Duration of placed drainage tube (days)	1.6 ± 1.8	1.3 ± 0.7	0.455
Total drain output (ml)	93.4 ± 428.5	33.2 ± 83.7	0.374
Perioperative complication	0.8	0.0	1.000

Transfusion: refers the total volume of autologous blood, allogeneic red blood cell, platelet, plasma and whole blood. Transfusion threshold stays the same during year 2014–2016.
FGHM: Flowable gelatin hemostatic matrix; HC: Historical control; LOS: Length of stay; SD: Standard deviation; TAH: Topical absorbable hemostatic agent.

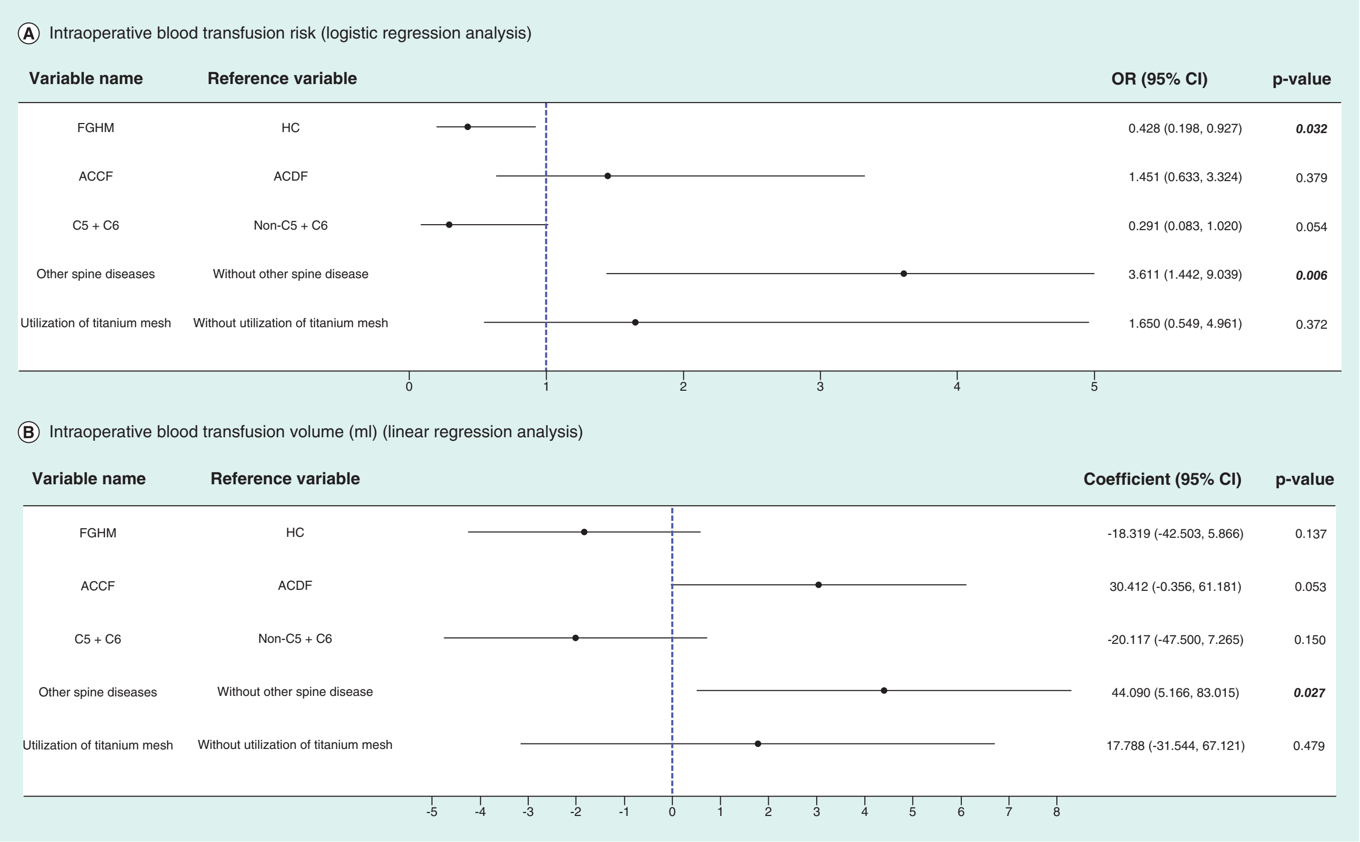

Figure 2. Risk factors of intraoperative transfusion by regression analysis.
ACCF: Anterior cervical corpectomy fusion; ACDF: Anterior cervical discectomy fusion; CI: Confidence interval; FGHM: Flowable gelatin hemostatic matrix HC: Historical control; OR: Odds ratio.

Table 3. Total hospital costs allocation in matched groups.

Variables	Matched FGHM group (n = 125)					Matched HC group (n = 125)					p-value
	Mean	Median	Q1	Q3	SD	Mean	Median	Q1	Q3	SD	
TAH	3155	3105	3095	3120	382	60	60	45	60	17	<0.001
Gelatin sponge	61	50	50	75	29	60	60	45	60	17	0.944
SURGIFLO®	3094	3045	3045	3045	384	0	0	0	0	0	<0.001
Implanted fixation	46,877	43,127	37,617	53,291	12,296	44,369	43,226	36,567	50,821	11,070	0.008
Disposable supplies	5368	5353	3365	6323	2236	7443	7325	5880	9391	2616	<0.001
Nursing	467	420	182	629	337	777	876	526	980	382	<0.001
Laboratory tests	2254	2070	1702	2481	927	2397	2225	1921	2674	752	0.021
Hospital bed	420	342	258	538	251	560	482	314	678	359	<0.001
Operation	3049	3061	2797	3097	310	3258	3153	2975	3396	552	<0.001
In-hospital dining	139	131	58	184	116	183	166	103	247	114	<0.001
Other therapy	129	114	97	142	62	191	140	122	174	401	<0.001
Personal care	12	3	2	18	16	18	9	3	29	21	0.009
Blood transfusion	30	0	0	0	175	49	0	0	67	108	<0.001
Medical image	1529	1331	984	2023	824	1155	1021	850	1451	606	<0.001
Anesthesia	545	558	531	586	69	524	558	503	586	106	0.341
Medicine	6043	5481	4543	6620	3864	5670	5286	4485	6959	1808	0.769
Others	17	4	4	4	25	26	4	4	49	53	0.087
Hospital costs, except TAH and implant fixation	20,002	19,214	17,115	21,616	6070	22,251	22,120	18,394	25,418	5033	<0.001
Hospitalization cost, except implant fixation	23,157	22,345	20,205	24,743	6134	22,311	22,165	18,454	25,463	5035	0.452
Total hospital costs	70,034	64,717	58,767	78,034	14,779	66,680	65,064	57,573	74,510	13,402	0.035

Average currency exchange during 2014 to 2016: US$1 ≈ 6.3378.
p-value: Wilcoxon test.
FGHM: Flowable gelatin hemostatic matrix; HC: Historical control; SD: Standard deviation; TAH: Topical absorbable hemostatic agent.

categories of hospital costs were observed, including disposable medical consumables (median ¥5353 vs ¥7325; $p < 0.001$), nursing (median ¥420 vs ¥876; $p < 0.001$), laboratory tests (median ¥2070 vs ¥2225; p = 0.021), and hospital bed (median ¥342 vs ¥482; $p < 0.001$). Therefore, the total reduced medical costs except TAH and implanted fixation in the matched FGHM patients was ¥2906 (median). The total hospital costs associated with the matched FGHM patients was lower than that in the matched HC patients with statistical significance (median ¥64,717 vs ¥65,064; p = 0.035). The results from generalized linear regression with adjustment for demographics, social economic status, lifestyle, type of procedure, operation site, utilization of fusion cage and titanium mesh and comorbidities were consistent with propensity score matching results: significantly lower total hospital costs subtracted cost of TAH and of implanted fixation (coefficient -0.050; p = 0.022) (Figure 3).

Variable name	Reference variable	Coefficient (95% CI)	p-value
FGHM	HC	-0.050 (-0.093, -0.007)	***0.022***
Age (years)		0.002 (-0.001, 0.004)	0.254
Beijing	Non-Beijing	0.082 (-0.077, 0.241)	0.315
Regional city	Non-regional city	0.025 (-0.019, 0.068)	0.269
Retired	Non-retired	0.057 (-0.010, 0.125)	0.097
Local public health insurance	New rural cooperative medical insurance	0.102 (-0.206, 0.410)	0.517
Military health insurance	New rural cooperative medical insurance	-0.035 (-0.463, 0.393)	0.871
Out-of-pocket expenses	New rural cooperative medical insurance	0.440 (0.100, 0.781)	***0.011***
Drinking	Non-drinking	0.099 (0.032, 0.167)	***0.004***
Previous treatment with anti-platelet/coagulants agents	No	0.273 (0.115, 0.431)	***< 0.001***
ACCF	ACDF	0.072 (0.010, 0.134)	***0.024***
C5 + C6	Non-C5 + C6	-0.007 (-0.075, 0.060)	0.830
C4 + C5 + C6 + C7	Non-C4 + C5 + C6 + C7	0.069 (-0.008, 0.147)	0.079
C6 + C7	Non-C6 + C7	-0.046 (-0.139, 0.048)	0.342
No-utilization of infusion Cage	Yes	0.052 (-0.093, 0.196)	0.482
1 Cage	> 1 Cage	-0.066 (-0.128, 0.005)	***0.034***
Utilization of titanium mesh	No	-0.030 (-0.154, 0.094)	0.634
Cardiovascular diseases	Without cardiovascular disease	0.074 (0.011, 0.136)	***0.021***
Cerebral infarction	Without cerebral infarction	-0.004 (-0.148, 0.140)	0.957
Cancer/tumor unrelated to spinal column	Without cancer / tumor related to spinal column	0.193 (-0.061, 0.446)	0.136

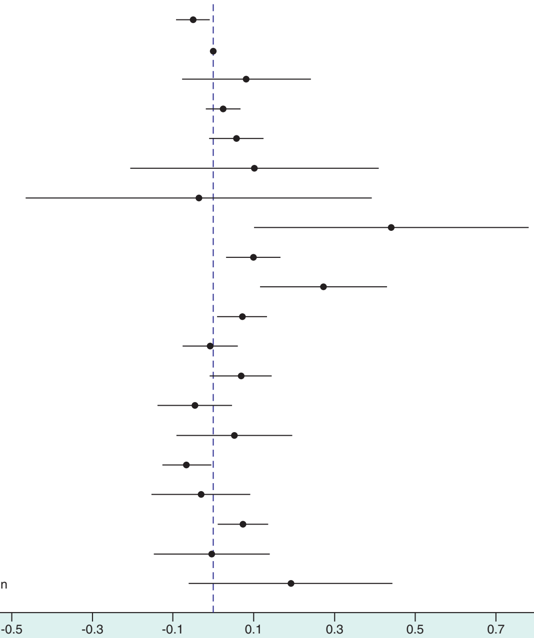

Figure 3. The impact of flowable gelatin hemostatic matrix on the hospital costs after the subtraction of the costs of hemostatic agents and implanted fixation in the included patients (n = 451).
ACCF: Anterior cervical corpectomy fusion; ACDF: Anterior cervical discectomy fusion; CVS: Cervical vertebrae surgery; FGHM: Flowable gelatin hemostatic matrix; HC: Historical control.

Discussion

The large volume of real-world cases of ACSS using FGHM (SURGIFLO) from 2015 to 2016 in our site allowed us to create sufficient propensity-score matched pairs and demonstrate the clinical and economic benefits associated with hemostasis. This is the first known study that assessed the impact of FGHM on cervical–spine perioperative benefits associated with hemostasis and hospital cost by using hospital medical records.

Every patient in the matched FGHM group received gelatin sponge but in significantly lower amounts compared with patients in matched HC group. According to the surgeons of the included patients, the gelatin sponge was usually used first for bleeding control in the FGHM group. Gelatin sponge can soak blood and provide a matrix for clot formation [13,14]. The spongey physical property renders it effective at stopping continuous oozing of visualized and even sites. However, it could be challenging when applying cauterization and high-swell TAH agents to stop bleeding of epidural veins, because these veins are a plexus of vessels surrounding the spinal cord and spinal nerves. Gelatin sponge is a mass-occupying agent and could considerably swell up once saturated with blood, which may potentially lead to neurological compression [15]. Flowable gelatin provides an environment for platelets to adhere and has a distinctly smaller swelling factor compared with gelatin sponge [7]. Also, flowable gelatin better conforms to irregular and deep surgical surface than performed nonflowable TAH agents [12,16]. These characteristics bring advantages to flowable gelatin for stopping venous bleeding from the spinal epidural space in ACSS when the conventional hemostatic agents did not work well in the first line setting. The lower amount of gelatin sponge in the matched FGHM group reflected that the improved hemostasis brought by FGHM reduced the needs of traditional hemostatic agents and offset some costs for gelatin sponge. Thus, the generated clinical evidence in our study confirmed that previously reported superior hemostasis effects of FGHM [17–20] could also occur in the Chinese setting.

Unlike a prospective study, patients in this observational study were not randomly assigned for treatment in clinical pathway. This limitation of retrospective studies necessitates other methods to minimize confounders on hemostatic agents and outcomes [21]. Therefore, this study applied propensity score matching to manage the treatment-selection bias. The low intraoperative blood transfusion rate and volume may be a result of the characteristics of ACSS. Compared with posterior lumbar spinal surgery, there is often less resection of the posterior longitudinal ligament in ACSS, causing less damage to tissue and blood vessel. Thus, the bleeding volume in ACSS was much less compared with the average 600 ml blood loss in lumbar spinal surgery [22]. The improved hemostasis effect of FGHM can also be supported by the statistical significance for the reduced operation time. When the anterior approach is used in cervical spinal discectomy, the operative field is narrow: mild intraoperative bleeding can reduce visibility, degrading accuracy and safety of the surgical technique. In other words, surgeons tend to conduct each step in the surgical procedure followed by prompt hemostasis, though it is time consuming. The prompt hemostasis achieved by FGHM could improve the flow and duration of procedure execution, which may bring better perioperative outcomes including shorter postsurgery LOS and lower risk of drainage tube placement. The operation time could have an impact on other outcomes, such as infection [23] and complications after hospital discharge [24], but these indicators were not measured in our study.

The cost of implanted fixation devices was separated mainly for two reasons: these devices in China are notably more expensive than other medical resources, and their prices vary from brand to brand. Cost of implanted fixation devices could be a confounder if the total medical cost is directly used for comparisons. Therefore, 'hospital costs, except cost of TAH and implanted fixation' was used to measure the economic impact associated with FGHM. This study showed that the cost savings associated with improved hemostasis by FGHM could offset the increased acquisition costs of FGHM (SURGIFLO). The comparisons of the cost distribution between matched groups showed that the reduction of medical costs in the matched FGHM group was driven primarily by the decreased cost of disposable medical consumables, which are mainly charged during blood transfusion and postsurgery care. For example, the lower requirement on intraoperative transfusion could result in less frequent usage of disposable blood-transfusion sets; the decreased risk for drainage could save the cost on disposable drainage tubes. Additionally, the economic impacts associated with the shortened postsurgery LOS was reflected through a lower cost of hospital bed, nursing service as well as laboratory tests that were used for postoperative infection and complications monitoring. Thus, this study could be a good example to demonstrate the economic impact associated with improved hemostasis. Though a significant reduction of blood transfusion in matched FGHM was observed, cost savings on blood transfusion were not observed, likely due to the already low blood transfusion rate/volume in ACSS and relatively low price of packed red blood cell (¥210/200 ml) in China. It also should be noted that the economic impact of reduced operation time associated with FGHM could be minimal because of the low service fee for operation rooms in China. This study also observed the costs of clinically relevant outcomes, including reduced blood transfusion, operation time, drainage tube placement and postsurgery LOS. Cost comparison results demonstrated that the increased cost for FGHM could be completely offset by the savings for other medical resources.

This study has limitations that could compound the generalizability of the results. First, this study was conducted in a single tertiary care hospital. Clinical outcomes associated with FGHM should be further explored in other medical settings. Second, due to the retrospective nature of this study, direct clinical measures, such as accurate bleeding volume to assess the hemostatic effects of FGHM, were not possible. Thus, future studies are needed to confirm the findings herein. Finally, our study excluded patients who received thrombin in surgery in order to minimize the potential confounding effects associated with thrombin in the control of bleeding. In real clinical practices, thrombin could be mixed with FGHM to further improve the hemostatic effects. Because the cost of thrombin is relatively low, future studies should further evaluate the hemostatic effects associated with FGHM mixed with thrombin that could gain more clinical and economic benefits.

In summary, this observational study identified a large number of propensity score-matched patients to demonstrate the favorable impact of FGHM on outcomes related to hemostasis in ACSS. Moreover, medical resources savings related to improved surgical outcomes could completely offset the acquisition costs of FGHM. These findings suggest that the adoption of FGHM beyond basic gelatin sponge would bring more favorable outcomes than gelatin sponge alone for hemostasis in ACSS. Future studies using direct outcome measures are warranted to confirm cost-effectiveness dominance of FGHM in ACSS.

Author contributions

Z Wang formulated the research idea and worked with Yunchang Wu; Yiqing Wu, G Gangoli, A Bourcet, W Danker III and W Chen drafted the study protocol, which was verified by Z Wang. Yunchang Wu and Q Gong coordinated the data acquisition. W Chen and H Zhan structured the collected data into the database, developed the data analysis plan, and conducted data analysis. Yunchang Wu and Z Wang interpreted the results from clinical perspective. Z Wang, Yunchang Wu, Yiqing Wu, G Gangoli, A

Bourcet, W Danker III and W Chen were fully involved with the development of this manuscript. All authors critically reviewed the manuscript and approved the submission of this manuscript.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval for this work.

Summary points

- Controlling epidural venous oozing during anterior cervical spine surgery is critical for the success of operation.
- Many studies have proven the efficacy of flowable gelatin hemostatic matrix (FGHM) in spinal surgery, but the economic impact of FGHM remains unclarified.
- The utilization of FGHM in anterior cervical spine surgery improved perioperative clinical outcomes.
- The use of FGHM did not increase overall hospital costs associated with anterior cervical spine surgery.
- The observed clinical and economic benefits associated with FGHM for anterior cervical spinal surgery support the introduction of FGHM for hemostasis in spine surgery.

References

1. Laratta JL, Shillingford JN, Saifi C *et al.* Cervical disc arthroplasty: a comprehensive review of single-level, multilevel, and hybrid procedures. *Global Spine J.* 8(1), 78–83 (2018).
2. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. *Eur. Spine J.* 13(Suppl. 1), s18–s27 (2004).
3. Shander A. Financial and clinical outcomes associated with surgical bleeding complications. *Surgery* 142(4S), S20–S26 (2007).
4. Corral M, Ferko N, Hollmann S *et al.* Health and economic outcomes associated with uncontrolled surgical bleeding: a retrospective analysis of the Premier Perspectives Database. *Clinicoecon. Outcomes Res.* 7, 409–421 (2015).
5. Emilia M, Luca S, Francesca B *et al.* Topical hemostatic agents in surgical practice. *Transfus. Apher. Sci.* 45(3), 305–311 (2011).
6. Sewlikar S, Rillai R, Mahajan N, Desai A. Bleeding scenarios in spine surgeries: role for tropical hemostatic agents. *J. Spinal Surg.* 2(1), 13–16 (2015).
7 . Gazzeri R, De Bonis C, Galarza M. Use of a thrombin–gelatin hemostatic matrix (SURGIFLO®) in spinal surgery. *Surg. Technol. Int.* 25, 280–285 (2014).
8. Comadoll JL, Comadoll S, Hutchcraft A *et al.* Comparison of hemostatic matrix and standard hemostasis in patients undergoing primary TKA. *Orthopedics* 35(6), e785–e793 (2012).
9. Tackett SM, Sugarman R, Kreuwel HT *et al.* Hospital economic impact from hemostatic matrix usage in cardiac surgery. *J. Med. Econ.* 17(9), 670–676 (2014).
10. Echave M, Oyagüez I, Casado MA. Use of Floseal®, a human gelatine–thrombin matrix sealant, in surgery: a systematic review. *BMC Surg.* 14(1), 111 (2014).
11. Helenius I, Keskinen H, Syvanen J *et al.* Gelatine matrix with human thrombin decreases blood loss in adolescents undergoing posterior spinal fusion for idiopathic scoliosis. *Bone Joint J.* 98(3), 395–401 (2016).
12. Renkens Jr KL, Payner TD, Leipzig TJ *et al.* A multicenter, prospective, randomized trial evaluating a new hemostatic agent for spinal surgery. *Spine* 26(15), 1645–1650 (2001).
13. Sileshi B, Achneck HE, Lawson JH. Management of surgical hemostasis: topical agents. *Vascular* 16(1 Suppl.), 22–28 (2008).
14. Schonauer C, Tessitore E, Barbagallo G *et al.* The use of local agents: bone wax, gelatin, collagen, oxidized cellulose. *Eur. Spine J.* 13(Suppl. 1), S89–S96 (2004).
15. Alander DH, Stauffer ES. Gelfoam-induced acute quadriparesis after cervical decompression and fusion. *Spine* 20(8), 970–971 (1995).
16. Cappabianca P, Esposito F, Esposito I *et al.* Use of a thrombin–gelatin haemostatic matrix in endoscopic endonasal extended approaches: technical note. *Acat. Neurochir.* 151, 69–77 (2009).
17. Gazzeri R, Galarza M, Alfier A. Safety biocompatibility of gelatin hemostatic matrix (Floseal and SURGIFLO®) in neurosurgical procedures. *Surg. Tech. Int.* 22, 49–54 (2012).

18. Gazzeri R, Galarza M, Neroni M, Alfieri A, Giordano M. Hemostatic matrix sealant in neurosurgery: a clinical and imaging study. *Acta Neurochir.* 153(1), 148–155 (2011).

19. Landi A, Gregori F, Marotta N, Delfini R. Efficacy, security, and manageability of gelified hemostatic matrix in bleeding control during thoracic and lumbar spine surgery: FloSeal versus Surgiflo. *J. Neurol. Surg. A Cent. Eur. Neurosurg.* 77(2), 139–143 (2016).

20. Price JS, Tackett S, Patel V. Observational evaluation of outcomes and resource utilization from hemostatic matrices in spine surgery. *J. Med. Economics* 18(10), 777–786 (2015).

21. Despotis GJ, Joist JH, Goodnough LT. Monitoring of hemostasis in cardiac surgical patients: impact of point-of-care testing on blood loss and transfusion outcomes. *Clin. Chem.* 43(9), 1684–1696 (1997).

22. Seraph V, Lerch C, Walochnik N *et al.* Comparison of conventional versus minimally invasive extraperitoneal approach for anterior lumbar interbody fusion. *Eur. Spine J.* 13, 425–431 (2004).

23. Eva YW, Cheung WY, Ng KF *et al.* Reducing perioperative blood loss and allogeneic blood transfusion in patients undergoing major spine surgery. *JBJS* 93(13), 1268–1277 (2011).

24. Wimmer C, Gluch H, Franzreb M *et al.* Predisposing factors for infection in spine surgery: a survey of 850 spinal procedures. *Clin. Spine Surg.* 11(2), 124–128 (1998).