Research Article

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Clinical and economic impact of oxidized regenerated cellulose for surgeries in a Chinese tertiary care hospital

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Aim: To assess the impact of oxidized regenerated cellulose (ORC) on blood transfusion and hospital costs associated with surgeries. **Patients & methods:** This retrospective cohort study selected ten surgeries to create propensity-score matching groups to compare ORC versus nonORC (conventional hemostatic techniques such as manual pressure, ligature and electrocautery). **Results:** NonORC was associated with both higher blood transfusion volume and higher hospital costs than ORC in endoscopic transnasal sphenoidal surgery, nonskull base craniotomy, hepatectomy, cholangiotomy, gastrectomy and lumbar surgery. However, nonORC was associated with better outcomes than ORC in open colorectal surgery, mammectomy and hip arthroplasty surgery. **Conclusion:** When compared with conventional hemostatic technique, using ORC could impact blood transfusion and hospital costs differently by surgical settings.

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Keywords: absorbable hemostatic agent • blood transfusion • Chinese • costs • oxidized regenerated cellulose • surgery

Bleeding is a common intraoperative complication increasing the risk of infection, postoperative complications and transfusion-related adverse events, which require longer hospital length of stay (LOS) and more health resources utilization [1,2]. Absorbable hemostatic agents (AHA) have been used as adjunctive therapy in surgeries when bleeding is not controlled by conventional methods [3]. Previous clinical evidence has suggested that AHA is effective in controlling capillary bleeding, achieving hemostasis during vascular surgery and controlling bleeding from fistula-puncture sites [4]. For example, oxidized regenerated cellulose (ORC), the most typical AHA, can assist in the control of capillary, venous and small arterial hemorrhage when ligation, electrocoagulation or other conventional methods to control bleeding are impractical or ineffective [5]. ORC facilitates hemostasis likely through the activation of the intrinsic coagulation pathway and also creating a gel-like layer (matrix) that holds clots in place and triggers vasoconstriction by the low pH of the ORC [6].

AHA is essentially needed for bleeding control in neurosurgery [7], hepatectomy [8], spine surgery [9] and vascular surgery [10]. Even though AHA has been used for two decades in China, AHA is rarely assessed for its impact on surgical outcomes and medical costs by surgery settings. Additionally, some Chinese hospitals had restricted the use of AHA irrespective of surgery setting to control budget since June 2016. This practice has raised concerns about the safety and quality of surgeries that are highly correlated with surgery bleeding [11]. With the recognition of the impact of using AHA on the safety and quality of surgery, the Chinese hospitals started to review the AHA restriction policy and seek evidence that could guide the appropriate use of AHA. Thus, this study selected one of the Chinese tertiary hospitals implementing AHA restriction use policy to clarify the impact of no AHA use on blood transfusion and hospital costs in common surgery settings.

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Patients & methods

This study selected a Chinese titer III tertiary care hospital, Xiangya Hospital, which did not supply ORC due to budget control in most surgeries since 1 June 2016, as the study setting to retrospectively identify hospital episodes before and after 1 June 2016 to assess the clinical and economic impact associated with ORC use in common surgery settings. Ethical approval was obtained from the Institutional Review Board of Xiangya Hospital.

Patient identification

This study retrospectively identified the patients who underwent ten types of surgeries before and after the stop of supplying ORC in Xiangya Hospital. The rank of the annual surgery volumes in the study hospital was used to guide the selection of surgical settings for the assessment. This study finally included ten surgery settings to identify eligible patients for assessment. These ten surgery settings included three neurosurgeries (endoscopic transnasal sphenoidal surgery [ESTSS], nonskull base craniotomy [NSBC] and cerebrovascular surgery [CVS]), five general surgeries (hepatectomy, open gastrectomy, cholangiotomy, open colorectal surgery and mammectomy) and two orthopedics surgeries (hip arthroplasty surgery and lumbar fusion surgery). The identified patients were further assessed for their eligibility according to the following inclusion and exclusion criteria. The inclusion criteria included the following: patients with age of 18 years or above; patients with using ORC in the above selected ten surgeries from 1 January 2015 to 31 May 2016, and patients without using ORC in the selected ten surgeries from 1 June 2016 to 31 December 2017; patients with general anesthesia for their surgeries; patients were routinely admitted from outpatient settings; and patients were routinely discharged from the study hospital. The patients will be excluded if any of the following criteria were met: patient medical records were missing or incomplete, patients had two or more irrelevant surgeries in the same hospital episode, patients had legal-defined viral diseases (viral hepatitis and human immunodeficiency virus), patients had coagulation disorders (such as hemophilia) and patients with top 2.5% of bleeding volume as the extremely high bleeding volume may due to unexpected circumstances during surgery (such as massive bleeding due to accidentally injuring the artery).

The patients using ORC in the selected ten surgeries from 1 January 2015 to 31 May 2016 were included to create the 'ORC group'. The patients without using ORC in the selected ten surgeries from 1 June 2016 to 31 December 2017 were included to create the 'nonORC group' after stopping the supply of ORC. The hemostasis methods used to control the bleeding in the surgery settings for the 'nonORC group' included manual pressure, ligation, electrocoagulation or other conventional hemostasis methods.

Data sources

The data sources in this study were the medical and billing records associated with the hospital episode of the surgeries in the included patients. The medical records included hospital medical summary sheet, surgery anesthesia records, surgical notes, medical notes and laboratory test results. The hospital medical summary sheet was used to extract patient demographics, socio-economic status, admission diagnoses, LOS, surgery methods, and complications. The anesthesia record was used to extract operation time. The surgical notes included information regarding surgery indication, operation site, procedure types, bleeding volume and intraoperative blood transfusion. The laboratory tests before surgery were used to extract the results of blood tests indicating bone marrow function and coagulation function. Additionally, the billing records were used to extract health resources utilization, including the use of blood for transfusion, and medical costs classified by categories.

Outcome measures

The primary outcome measures in this study were the occurrence of intraoperative blood transfusion, blood transfusion volume (based on the used blood units from the billing records, one blood unit was 200 ml), operation time and postsurgery LOS. This study also included hospital costs to clarify the economic impact of restricting ORC use. All costs were adjusted to 2017 Chinese currency according to the Chinese National Consumer Price Index from 2016 to 2017 [12].

Data analysis

This study stratified the patients by ten surgical settings to conduct the following analysis and assessed the impact of not using ORC on the measured outcomes through comparisons with using ORC. The created 'ORC group' and 'nonORC group' for each surgery setting were included to conduct the following analyses. This study used the propensity-score methods for adjusted comparisons of the measured outcomes associated with the created two groups. The patient baseline characteristics of the two groups were compared with the Student's t-test or chi-square test to identify the patient characteristics with significant differences between the two groups. These identified patient characteristics were further used to create propensity-score matched groups to compare measured outcomes. The created propensity-score matched groups were compared by using paired Student's t-test for continuous outcomes, McNemar test for categorical outcomes and Wilcoxon signed-rank test for hospital costs. Statistical software R was used to perform the data analysis described above. The statistical significance in the performed data analyses was defined as a two-sided p-value less than 0.05.

Results

This study initially identified 15,537 patients who underwent the selected ten surgeries from the two defined time windows. After inclusion and exclusion, a total of 5323 patients were included to create propensity score-matched groups for nonORC group versus ORC group for the ten selected surgeries, respectively. The patient identification process from initial screening to creating propensity-score matched groups for the selected ten surgeries is summarized in Table 1.

Comparisons of the outcome measures associated with the nonORC group versus ORC group in neurosurgeries

This study created 101 propensity-score matched pairs for ESTSS, 270 propensity-score matched pairs for NSBC and 81 propensity-score matched pairs for CVS. The patient baseline characteristics and measured outcomes of the created propensity-score matched pairs for the three selected neurosurgeries are summarized in Table 2. The matched pairs for the three selected neurosurgeries were well balanced, not demonstrating any significant differences in patient demographics, bone marrow function, primary surgery indications and main comorbidities. Further comparisons for the three selected neurosurgeries identified that the matched nonORC group was associated with both higher blood transfusion volume and hospital costs than the matched ORC group in ESTSS (20.0% higher for blood transfusion volume: 120.2 ± 550.2 ml vs 100.2 ± 552.0 ml, p = 0.799; 7.4% higher for the mean hospital costs: ¥88,101 ± 34,900 vs ¥82,046 ± 29,776, p = 0.101) and NSBC (19.0% higher for blood transfusion volume: 303.6 ± 845.0 ml vs 255.1 ± 539.3 ml, p = 0.427; 13.2% higher for the mean hospital costs: ¥109,774 ± 58,673 vs ¥96,991 ± 48,237, p = 0.002). When compared with the matched ORC group, the matched nonORC group was associated with a lower intraoperative blood transfusion rate (26.4% lower: 30.9 vs 42.0%, p = 0.164) and blood transfusion volume (19.8% lower: 172.9 ± 409.4 ml vs 215.7 ± 405.2 ml, p = 0.509) in CVS. However, the mean hospital costs in the matched nonORC group were 8.7% higher than that for the matched ORC group (¥118,444 ± 51,371 vs ¥108,957 ± 55,829, p = 0.156) in CVS. The other measured outcomes, including operation time and post-surgery hospital length, associated with the created propensity-score matched pairs for the three selected neurosurgeries were comparable.

Comparisons of outcome measures associated with nonORC group versus ORC group in general surgeries

This study created propensity-score matched pairs for five selected general surgeries, which included hepatectomy (93 pairs), biliary resection surgery (41 pairs), gastrectomy (111 pairs), proctocolectomy (86 pairs) and breast surgery (261 pairs). The patient baseline characteristics and measured outcomes of the matched pairs for the five selected general surgeries are summarized in Table 3. The matched pairs were well balanced in their patient baseline characteristics without any significant differences in patient demographics, primary surgery indications, bone marrow function and primary comorbidities. The comparisons observed that the matched nonORC group was associated with higher mean blood transfusion volume in hepatectomy (16.4% higher: 465.3 ± 1238.6 ml vs 399.6 ± 909.8 ml, p = 0.692), cholangiotomy (165.1% higher: 213.4 ± 999.8 ml vs 80.5 ± 292.6 ml, p = 0.329) and gastrectomy (25.0% higher: 325.3 ± 940.1 ml vs 260.2 ± 701.1 ml, p = 0.574) than the matched ORC group. Additionally, the matched nonORC group was associated with higher mean hospital costs in hepatectomy (11.4% higher: ¥128,061 ± 92,950 vs ¥114,959 ± 76,535, p = 0.287), cholangiotomy (30.3% higher: ¥134,996 ± 65,603 vs ¥103,580 ± 48,408, p = 0.031) and open gastrectomy (20.1% higher: ¥91,209 ± 50,353 vs ¥75,971 ± 34,462, p = 0.035). However, the matched nonORC group was associated with an increase in neither blood transfusion volume nor hospital costs in proctocolectomy and breast surgery.

Table 1. Summary of patient identification process to create propensity-score matched patients for stopping the use of oxidized regenerated cellulose versus using oxidized regenerated cellulose in the ten selected surgeries.

Surgery category		Selected neurosurgeries			Selected general surgeries					Selected bone surgeries	
Surgery method		Endoscopic transnasal sphenoidal surgery	Nonskull base craniotomy	Cerebrovascular surgery	Hepatectomy	Open gastrectomy	Cholangiotomy	Open colorectal surgery	Mammectomy	Hip arthroplasty surgery	Lumbar surgery
Initially identified patients		941	2378	1768	800	965	737	654	4134	1059	2101
Patent exclusion reasons	Age under 18 years	29	122	64	0	2	1	3	53	0	22
	Admission not from the outpatient setting	22	112	846	11	23	55	18	6	45	41
	Nonroutine discharge	6	50	27	3	4	3	4	1	6	49
	Not general anesthesia	1	5	1	1	2	2	0	1463	546	8
	Missing or incomplete information	175	397	113	88	179	140	113	402	47	554
	Legally reported viral diseases	29	83	25	166	51	33	29	57	20	99
	More than one surgery indication	25	60	8	69	8	133	6	1	3	10
	Patients without using ORC from 1 January 2015 to 31 May 2016, and patients with using ORC from 1 June 2016 to 31 December 2017	143	436	200	113	193	167	165	643	179	554
	Platelet infusion in surgery	10	20	15	7	5	3	1	3	2	11
	Extremely high blood transfusion volume	102	55	29	52	18	15	12	114	49	118
Patients used to create propensity-score matched groups		399	1038	440	290	480	185	303	1391	162	635
Propensity-score matched pairs		101	270	81	93	111	41	86	261	20	52

ORC: Oxidized regenerated cellulose.

Table 2. Patient baseline characteristics and measured outcomes of the created propensity-score matched patients for the three selected neurosurgeries.

Surgery type	Endoscopic transnasal sphenoidal surgery			Nonskull base craniotomy			Cerebrovascular surgery		
	nonORC group (n = 101)	ORC group (n = 101)	p-value	nonORC group (n = 270)	ORC group (n = 270)	p-value	nonORC group (n = 81)	ORC group (n = 81)	p-value
Patient baseline characteristics									
Age (years)	48.5 ± 12.6	47.0 ± 11.7	0.377	49.5 ± 12.3	50.8 ± 11.9	0.176	45.5 ± 12.6	49.0 ± 13.7	0.099
Male (%)	42.6%	42.6%		41.9%	41.9%		40.7%	53.1%	
Primary surgery indication									
Pituitary tumor (%)	89.1%	86.1%	0.248				1.2%	1.2%	1.000
Meningioma (%)				43.3%	43.0%	1.000			
Glioma (%)				46.3%	47.0%	0.480			
Hemangioblastoma (%)							40.7%	40.7%	1.000
Aneurysm (%)							34.6%	29.6%	0.556
Arteriovenous malformation (%)							16.0%	17.3%	1.000
Bone marrow function									
Normal INR (%)	97.0%	99.0%	0.617	99.6%	98.5%	0.371	96.3%	96.3%	1.000
Normal red blood cell counts (%)	80.2%	80.2%	1.000	85.2%	88.5%	0.313	81.5%	74.1%	0.377
Normal hemoglobin (%)	78.2%	81.2%	0.248	88.1%	87.8%	1.000	79.0%	82.7%	0.710
Normal platelet counts (%)	92.1%	95.0%	0.579	94.1%	93.7%	1.000	93.8%	92.6%	1.000
Main comorbidities									
Hypertension (%)	10.9%	13.9%	0.689	10.0%	12.6%	0.427	2.5%	2.5%	1.000
Diabetes (%)	2.0%	2.0%	1.000	3.3%	2.6%	0.803	1.2%	2.5%	1.000
Cerebrovascular diseases (%)	3.0%	3.0%	1.000	1.1%	3.3%	0.114	27.2%	14.8%	0.066
Measured outcomes									
Intraoperative transfusion rate (%)	9.9%	6.9%	0.606	30.4%	33.0%	0.562	30.9%	42.0%	0.164
Total transfusion volume (ml)	120.2 ± 550.2	100.2 ± 552.0	0.799	303.6 ± 845.0	255.1 ± 539.3	0.427	172.9 ± 409.4	215.7 ± 405.2	0.509
Operation time (h)	4.3 ± 1.8	4.5 ± 1.9	0.550	6.4 ± 2.2	6.4 ± 2.4	0.895	6.0 ± 1.9	6.4 ± 3.0	0.269
Postoperative LOS (days)	9.9 ± 4.4	9.4 ± 5.3	0.436	13.7 ± 7.1	13.2 ± 6.8	0.313	12.5 ± 4.8	12.8 ± 6.0	0.755
Hospital costs (RMB)			0.101			**0.002**			0.156
Mean ± SD	88,101 ± 34,900	82,046 ± 29,776		109,774 ± 58,673	96,991 ± 48,237		118,444 ± 51,371	108,957 ± 55,829	
Median	91,701	84,953		93,806	82,582		114,057	94,293	

Characteristics and outcomes were described as mean ± standard deviation or percentage as appropriate.
The bold digits signifies the p-value less than 0.05.
LOS: Length of stay; INR: International normalized ratio; ORC: Oxidized regenerated cellulose; SD: Standard deviation.

Table 3. Patient baseline characteristics and measured outcomes of the created propensity-score matched patients for the five selected general surgeries.

Patient characteristics	Hepatectomy			Cholangiotomy			Open gastrectomy		
	nonORC group (n = 93)	ORC group (n = 93)	p-value	nonORC group (n = 41)	ORC group (n = 41)	p-value	nonORC group (n = 111)	ORC group (n = 111)	p-value
Patient baseline characteristics									
Age (years)	53.2 ± 10.7	52.5 ± 11.5	0.665	55.1 ± 11.9	54.5 ± 11.9	0.814	56.7 ± 11.5	53.9 ± 12.4	0.081
Male (%)	52.70%	49.50%	0.749	39.00%	43.90%	0.823	73.00%	63.10%	0.170
Primary surgery indication									
Malignant tumors (%)	62.40%	54.80%	0.281	7.30%	19.50%	0.228	89.20%	91.00%	0.823
Stone (%)	14.00%	14.00%	1.000	68.30%	58.50%	0.522			
Benign tumors (%)	15.10%	21.50%	0.307	2.40%	4.90%	1.000	4.50%	1.80%	0.450
Bone marrow function									
Normal INR (%)	93.50%	96.80%	0.505	92.70%	97.60%	0.617	94.60%	97.30%	0.450
Normal red blood cell counts (%)	68.80%	68.80%	1.000	70.70%	61.00%	0.502	61.30%	68.50%	0.332
Normal hemoglobin (%)	71.00%	72.00%	1.000	63.40%	75.60%	0.332	55.90%	56.80%	1.000
Normal platelet counts (%)	83.90%	76.30%	0.265	90.20%	87.80%	1.000	82.90%	84.70%	0.855
Primary comorbidities									
Hypertension (%)	3.20%	3.20%	1.000				9.90%	3.60%	0.121
Coronary heart disease (%)									
Diabetes (%)							2.70%	4.50%	0.724
Cerebrovascular diseases (%)	0.00%	1.10%	1.000				2.70%	0.90%	0.617
Measured outcomes									
Intraoperative transfusion rate (%)	19.40%	17.20%	0.838	4.90%	4.90%	1.000	19.80%	21.60%	0.871
Total transfusion volume (ml)	465.3 ± 1238.6	399.6 ± 909.8	0.692	213.4 ± 999.8	80.5 ± 292.6	0.329	325.3 ± 940.1	260.2 ± 701.1	0.574
Operation time (h)	4.6 ± 1.3	4.6 ± 1.6	0.739	3.5 ± 1.4	3.8 ± 1.9	0.335	4.5 ± 1.6	4.0 ± 1.4	0.033
Postoperative LOS (days)	13.8 ± 8.9	13.7 ± 10.2	0.921	12.5 ± 6.9	12.2 ± 3.8	0.834	12.4 ± 6.0	12.9 ± 5.4	0.516
Total hospital costs (RMB)			0.287			0.031			0.035
Mean ± SD	128,061 ± 92,950	114,959 ± 76,535		134,996 ± 65,603	103,580 ± 48,408		91,209 ± 50,353	75,971 ± 34,462	
Median	99,430	98,971		117,835	101,748		68,409	65,852	

Characteristics and outcomes were described as mean ± standard deviation or percentage as appropriate.
INR: International normalized ratio; LOS: Length of stay; ORC: Oxidized regenerated cellulose; SD: Standard deviation.

Table 3. Patient baseline characteristics and measured outcomes of the created propensity-score matched patients for the five selected general surgeries (cont.).

	Open colorectal surgery			Mammectomy		
	nonORC group (n = 86)	ORC group (n = 86)	p-value	nonORC group (n = 261)	ORC group (n = 261)	p-value
Patient baseline characteristics						
Age (years)	55.8 ± 10.2	57.9 ± 14.0	0.252	50.0 ± 10.3	49.9 ± 10.0	0.788
Male (%)	50.00%	50.00%	1.000	0.80%	0.40%	1.000
Primary surgery indication						
Malignant tumors (%)	86.00%	89.50%	0.646	95.40%	94.60%	0.724
Benign tumors (%)	5.80%	5.80%	1.000			
Bone marrow function						
Normal INR (%)	100.00%	100.00%	1.000	97.30%	96.60%	0.724
Normal red blood cell counts (%)	75.60%	75.60%	1.000	62.50%	70.90%	0.068
Normal hemoglobin (%)	61.60%	58.10%	0.700	68.20%	72.00%	0.411
Normal platelet counts (%)	77.90%	83.70%	0.383	91.60%	88.50%	0.312
Primary comorbidities						
Hypertension (%)	10.50%	12.80%	0.814	8.00%	8.00%	1.000
Coronary heart disease (%)				0.80%	0.40%	1.000
Diabetes (%)	1.20%	2.30%	1.000	1.10%	1.90%	0.724
Cerebrovascular diseases (%)	1.20%	2.30%	1.000	0.80%	0.00%	0.617
Measured outcomes						
Intraoperative transfusion rate (%)	4.70%	12.80%	0.096	0.00%	0.80%	0.617
Total transfusion volume (ml)	56.6 ± 175.0	125.6 ± 438.8	0.183	0.9 ± 13.9	2.3 ± 26.2	0.414
Operation time (h)	3.5 ± 1.3	3.3 ± 1.0	0.183	2.9 ± 0.6	3.0 ± 0.7	0.150
Postoperative LOS (days)	11.0 ± 5.5	13.4 ± 10.0	0.053	11.3 ± 2.9	11.3 ± 2.9	0.545
Total hospital costs (RMB)			0.005			0.000
Mean ± SD	60,113 ± 36,126	65,806 ± 40,244		33,090 ± 12,754	37,457 ± 17,071	
Median	51,583	58,553		30,956	33,924	

Characteristics and outcomes were described as mean ± standard deviation or percentage as appropriate.
INR: International normalized ratio; LOS: Length of stay; ORC: Oxidized regenerated cellulose; SD: Standard deviation.

Table 4. Patient baseline characteristics and measured outcomes of the created propensity-score matched patients for the two selected bone surgeries.

Patient characteristics	Lumbar surgery			Hip arthroplasty surgery		
	nonORC group (n = 52)	ORC group (n = 52)	p-value	nonORC group (n = 20)	ORC group (n = 20)	p-value
Patient baseline characteristics						
Age (years)	52.8 ± 14.3	51.9 ± 12.4	0.740	56.8 ± 10.5	55.8 ± 12.8	0.666
Male (%)	51.90%	48.10%	0.850	50.00%	50.00%	1.000
Primary surgery indication (%)						
Fracture (%)	0.00%	1.90%	1.000	15.00%	10.00%	1.000
Lumbar degeneration (%)	98.10%	96.20%	1.000			
Osteoarthritis (%)				15.00%	15.00%	1.000
Osteonecrosis of the femoral head (%)				55.00%	55.00%	1.000
Ankylosing spondylitis (%)				5.00%	10.00%	1.000
Bone marrow function						
Normal INR (%)	98.10%	100.00%	1.000	100.00%	100.00%	1.000
Normal red blood cell counts (%)	82.70%	86.50%	0.803	85.00%	75.00%	0.683
Normal hemoglobin (%)	75.00%	84.60%	0.383	85.00%	70.00%	0.505
Normal platelet counts (%)	94.20%	98.10%	0.617	75.00%	75.00%	1.000
Primary comorbidities						
Hypertension (%)	1.90%	3.80%	1.000	20.00%	10.00%	0.683
Diabetes (%)	3.80%	3.80%	1.000			
Measured outcomes						
Intraoperative transfusion rate (%)	84.60%	51.90%	0.001	80.00%	80.00%	1.000
Total transfusion volume (ml)	494.7 ± 589.6	286.2 ± 388.5	0.028	511.5 ± 453.1	619.0 ± 623.5	0.936
Operation time (h)	4.1 ± 1.2	4.5 ± 1.3	0.181	2.8 ± 0.7	3.2 ± 1.1	0.231
Postoperative LOS (days)	12.1 ± 3.2	13.2 ± 5.1	0.285	10.1 ± 4.0	9.3 ± 3.2	0.409
Hospital costs (RMB)			0.253			0.522
Mean ± SD	176,191 ± 79,534	159,321 ± 80,186		112,890 ± 35,641	114,196 ± 64,656	
Median	169,886	160,052		99,148	98,321	

Characteristics and outcomes were described as mean ± standard deviation or percentage as appropriate.
INR: International normalized ratio; LOS: Length of stay; ORC: Oxidized regenerated cellulose; SD: Standard deviation.

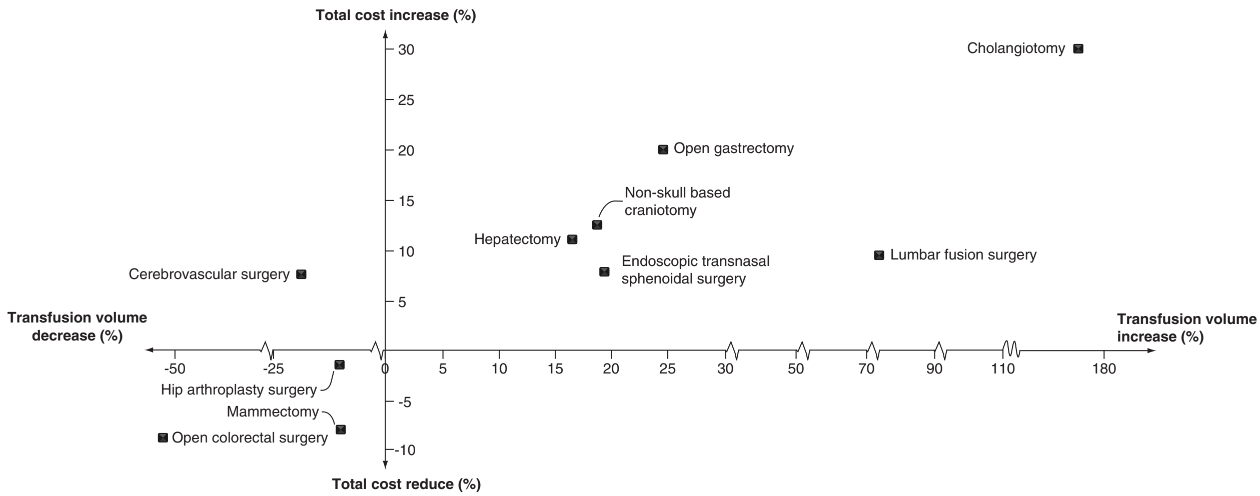
Comparisons of the outcome measures associated with the nonORC group versus ORC group in orthopedics surgeries

In lumbar surgery (52 pairs) and hip arthroplasty surgery (20 pairs), the matched groups were well balanced in their demographics, primary surgical indicators, bone marrow function and comorbidities (Table 4). The comparisons of the outcomes observed that the matched nonORC was associated with significantly higher intraoperative blood transfusion rate (63.0% higher: 84.6 vs 51.9%, p = 0.001) and significantly higher blood transfusion volume (72.9% higher: 494.7 ± 589.6 ml vs 286.2 ± 388.5 ml, p = 0.028) than the matched ORC group in lumbar surgery. Additionally, the matched nonORC group was associated with slightly higher hospital costs than the matched ORC group in lumbar surgery (10.6% higher: ¥176,191 ± 79,534 vs ¥159,321 ± 80,186, p = 0.253).

The changes in mean blood transfusion volume and mean hospital costs for the matched two groups in the ten surgery settings were plotted in Figure 1.

Discussion

This study mainly assessed the real-world impact of ORC as an adjunct therapy for bleeding control in ten surgeries that were commonly conducted in Chinese tier III hospitals. This study observed a higher transfusion rate/volume and higher hospital costs in the nonORC group in six of the selected ten surgeries, which included ESTSS, NSBC, hepatectomy, cholangiotomy, open gastrectomy and lumbar surgery. Thus, these six surgeries would gain more clinical benefits if using AHA. As hospital LOS and blood transfusion associated with surgeries usually decrease with improved quality of hospital care over time, the prolonged hospital LOS or increased blood transfusion associated



Surgery methods	Endoscopic transnasal sphenoidal surgery	Non-skull base craniotomy	Cerebrovascular surgery	Hepatectomy	Cholangiotomy	Open gastrectomy	Open colorectal surgery	Mammectomy	Lumbar surgery	Hip arthroplasty surgery
Mean blood transfusion volume change (%)	20.0%	19.0%	-19.8%	16.4%	165.1%	25.0%	-54.9%	-60.9%	72.9%	-17.4%
Mean total hospital costs change (%)	7.4%	13.2%	8.7%	11.4%	30.3%	20.1%	-8.7%	-11.7%	10.6%	-1.1%

Figure 1. The plotted changes of mean blood transfusion volume and median hospital costs associated with the created propensity-score matched groups for nonoxidized regenerated cellulose group versus oxidized regenerated cellulose group in the selected ten surgeries.

with the ‘nonORC group’, which was identified in the latest time window, might be the indicators of deteriorating quality of hospital care after the restrict use of AHA in Chinese tertiary care hospitals.

Diligent and meticulous bipolar electrocautery is the main method to achieve hemostasis in neurosurgeries [13], while ORC could quickly aid in the hemostasis of slow venous and capillary ooze associated with the excision of intrinsic tumors, lobectomy or the removal of intracerebral hemorrhage [7]. The adjunctive hemostasis effects of ORC could be confounded by the complexity of surgical procedures and were unlikely to be fully demonstrated by the indirect outcome measures [14]. However, this study observed the relatively higher blood transfusion volume and higher hospital costs in the nonORC group in NSBC, which demonstrated the clinical and economic benefits of using ORC as the adjunct hemostasis. Similar findings were also observed in ESTSS, which requires clear visualization under endoscopy. The applications of ORC to control oozing may enhance the visualization in ESTSS [15]. As for CVS, this study observed higher blood transfusion volume, but lower hospital costs in the ORC group. This inconsistency might be caused by unknown confounders, such as the use of other techniques that could decrease blood transfusion but cost more.

Of the selected five general surgeries, hepatectomy could have the highest risk of bleeding due to the hepatic sinusoidal structure of the liver, in which there is no smooth muscle to control bleeding through vasoconstriction [16]. When using conventional hemostasis methods, including suturing and ligation, it is hard to manage multiple bleeding sites on the wide and raw surfaces of the liver after the parenchymal lacerations [17]. Similarly, radical surgery for gastric cancer could leave multiple bleeding sites, while ORC might provide suitable adjunct hemostasis through wrapping [18]. Hence, hepatectomy, open gastrectomy and cholangiotomy could obtain more clinical and economic benefits, indicated by lower blood transfusion and lower hospital costs, through using ORC. The other two general surgeries, proctocolectomy and breast resection surgery, were associated with neither higher blood transfusion volume nor higher total hospitalization cost after the stop of using ORC. The assessment of the clinical and economic impact of restricting the use of ORC in these five selected general surgeries confirmed the need for guidance regarding the appropriate use of ORC by surgery setting.

This study assessed the needs of the appropriate use of ORC in lumbar surgery and hip arthroplasty surgery. This study observed a significantly higher intraoperative blood transfusion rate and also blood transfusion volume in the matched nonORC group in lumbar surgery. Because bipolar cautery can induce thermal injury to adjacent nerve roots in spine surgery, this finding was likely to support the use of ORC, which could better control the epidural oozing during spinal surgery [19]. Though previous research reported that using ORC to fill the bone surface and soft tissue gap before incision closure can effectively reduce hidden blood loss in hip arthroplasty surgery [20], our study did not observe any improved outcomes for blood transfusion or lower hospital costs in the ORC group. Because hip arthroplasty surgery was associated with 80% of the intraoperative blood transfusion rate and the mean total blood transfusion volume above 500 ml, the adjunct hemostasis effects associated with ORC were unlikely to sufficient in hip arthroplasty surgery.

The observed variances of blood transfusion and hospital costs associated with ORC in the selected ten surgeries in this study were well aligned with the hemostasis mechanisms of ORC. For example, (Surgicel, Ethicon, Inc. NJ, USA) the ORC used in our hospital setting, is made of sterile cellulose-based thrombogenic material that can control bleeding originating from delicate and/or friable tissues. Because Surgicel is shaped as a gauze-like material and is easily inserted into the areas that are difficult to reach, Surgicel could be a more practical option to reach the narrow surgical spaces and areas than conventional hemostatic methods for the control of the bleeding. Additionally, Surgicel can form a gelatinous mass upon saturation with blood and create a stable clot, which is highly effective in control massive bleeding associated with the surgical surface. Thus, the better hemostasis effects associated with Surgicel, indicated by the reduced blood transfusion, in ESTSS, NSBC, hepatectomy, cholangiotomy, gastrectomy and lumbar surgery supported the use of ORC to address those hemostasis challenges in surgeries.

Most of our study results are well aligned with the expected correlation between blood transfusion and hospital costs (more blood transfusion drove up hospital costs). However, this study observed the opposite correlation between blood transfusion volume and hospital costs in CVS. We have carefully reviewed the patient characteristics of the created propensity-score matched groups for ORC versus nonORC in this surgery. Even though most patient characteristics were well balanced in the matched group, the matched nonORC group was associated with a doubled rate of cerebrovascular diseases when compared with the matched ORC group (27.2 vs 14.8%, $p = 0.066$). Because cerebrovascular diseases are well-recognized contributors to medical costs [21], CVS in these patients could consume more hospital resources to stabilize the conditions of cerebrovascular disease before surgery. Additionally, there could be other unknown patient characteristics with strong confounding effects introducing bias in the comparisons. For example, the socio-economic status is always a strong confounder for hospital costs in Chinese real-world hospital settings [22]. However, the socio-economic status information in the hospital records was limited and incomplete. Thus, the impact of clinical benefits associated with ORC on hospital costs could not be fully clarified and demonstrated.

As a retrospective cohort study, the lack of reliable outcome measures to directly assess the adjunct hemostasis effects associated with ORC was the primary limitation in this study. This study selected a proven indirect outcome measure, blood transfusion volume, to measure hemostasis effects. Thus, the actual adjunct hemostasis associated with using ORC in this study could be discounted by the indirect outcome measure. Additionally, the bleeding risk associated with the same surgery could vary substantially by the complexity of surgery procedures. This study did not collect sufficient information for the surgical procedures to adjust their confounding effects in the comparisons of propensity score-matched groups. For example, colorectal resection surgery for colon cancer could experience a much higher risk of bleeding in the advanced cancer stage, which requires expanding the surgical cut area and lymphatic clearance. Moreover, the admission periods of the nonORC group and ORC group were sequential. The confounding effects associated with hospital care quality overtime on the measured outcomes could not be adjusted either in this study. Finally, this study did not adjust the surgeons in the propensity score comparisons due to the small sample size while the surgeon's skills play crucial roles in surgery bleeding control. Finally, most comparisons between the propensity score-matched groups only observed a nonsignificant trend for the clinical and economic benefits associated with ORC likely due to the small sample size. Given the limitations listed above, future studies are still needed to conduct a randomized clinical trial with sufficient sample size and outcome measures directly assessing hemostasis effects to draw more definitive conclusions for ORC in these surgery settings.

Conclusion

This study observed increased blood transfusion and hospital costs in specific surgery settings in a Chinese tertiary care hospital which used conventional hemostatic techniques without ORC. More specifically, not using ORC would increase the burden of transfusion and total hospital costs in ESTSS, NSBC, hepatectomy, cholangiotomy, gastrectomy and lumbar surgery. Thus, using ORC for adjunct hemostasis in these surgery settings should be encouraged to address their hemostasis needs.

Summary points

- Oxidized regenerated cellulose (ORC) could gain more clinical and economic benefits than conventional hemostatic methods in the surgeries with hemostasis challenges due to narrow surgical space and massive bleeding.
- The varied clinical and economic outcomes associated with ORC across surgery settings indicated the needs of evidence-based clinical decision making regarding the use of ORC in surgeries.
- Blood transfusion could be a reasonable outcome measure indirectly assessing hemostasis effects in real-world surgery settings.
- It is challenging to fully control the known and unknown confounding effects in retrospective cohort studies assessing hemostasis effects associated with ORC.
- Randomized control trial could be a better study design to achieve definitive conclusions on the hemostasis effects of ORC.

Author contributions

Z Qian and W Chen formulated the research idea and developed the study protocol. F Xiong, X Xia, P Gu, Q Wang and A Wu developed data extraction strategies, coordinate the data access and conducted data extraction from the hospital information system. Q Gong, Y Chen and H Zhan followed the study protocol to clean the extracted data and perform the data analysis. Z Qian and W Chen drafted the manuscript. All authors have critically reviewed the manuscript and approved this manuscript submission.

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