Reduced Postoperative Bleeding Following Use of Tisseel Fibrin Sealant in 300 Patients Undergoing Open-Heart Surgery

T. M. KIESER, A. MAITLAND, L. PARSONS, L. DAVISON, and R. C. WOODMAN

Abstract

The ability of Tisseel fibrin sealant to control bleeding was evaluated in this retrospective study. A new cardiac surgical unit was opened at the Foothills Hospital in Calgary, Alberta, in September 1988. Bleeding problems associated with its development led to a policy, instituted in late February 1989, of using Tisseel on all open-heart patients. Three hundred patients were reviewed in this study: 100 consecutive patients prior to the use of Tisseel (group I), 100 consecutive patients immediately following the initial use of Tisseel (group II), and 100 consecutive patients 1 year later (group III). These groups allowed the evaluation of Tisseel's effectiveness in light of possible learning curves as the surgical unit developed. No significant differences in age, sex, type of surgery performed, use of hypothermia, pump time, or cross-clamp time were found among the three groups. A significantly higher percentage of patients in group III, the late Tisseel group, underwent urgent or emergent surgery. The use of Tisseel, both initially (group II) and 1 year later (group III), was found to result in significant reductions in the number of units transfused during surgery, chest tube drainage within the first 24 h after surgery, and total chest tube drainage. The reoperation rate for bleeding was also significantly reduced when Tisseel was used, both initially (group II) and 1 year later (group III). Finally, the percentage of patients requiring no blood products during open-heart surgery increased dramatically with the use of Tisseel (groups II and III compared to group I). Comparison of blood product use in the two Tisseel groups yielded no significant differences. This suggests that Tisseel, rather than a learning curve, greatly benefited our patients with regards to bleeding in cardiac surgery.

Introduction

Complications associated with bleeding in cardiac surgery patients pose a considerable hazard to an already critically ill population. Such complications include the requirement for reoperation for bleeding, excessive blood product administration, and transmission of transfusion-related disease [1].

A new cardiac surgical unit was opened at the Foothills Hospital in Calgary, Alberta, in September 1988. From the outset, strict criteria for reoperation due to bleeding were maintained. Patients who lost more than 500 cc blood in 1 h, or who experienced repeated 200 cc/h blood loss for several hours underwent reoperation to identify the bleeding source. It soon became apparent that this unit was experiencing an inordinately high rate of reoperation for bleeding, nearly 22 %, compared to the ideal rate of 1 %–2 % [2]. In addition, patients were receiving an average of 6.8 U packed cells, compared to 1–3 U reported in the literature [3, 4].

This serious situation was addressed in February 1989 by the implementation of a policy to use Tisseel fibrin sealant, in the form of 5 cc topical spray, on all open-heart patients. The situation at Foothills Hospital was somewhat unique. In most institutions fibrin sealants are used only on high-risk patients or those experiencing excessive bleeding during surgery [5, 6]. At Foothills Hospital from February 1989 to September 1990 every open-heart patient received Tisseel. Concomitant with its use the reoperation for bleeding rate appeared to decline, as did the use of blood products and chest tube losses. The purpose of this retrospective study was to support these clinical observations and to evaluate whether they were due to the learning curve of the staff in a developing cardiac surgical unit or to changes in patient characteristics over this time period.

Patients included those prior to the use of Tisseel (group I), those immediately following the use of Tisseel (group II), and those 1 year later (group III). It was hypothesized that if a learning curve was responsible for the noted improvements, a general trend towards improvement over time and significant differences between group II and group III would be evident. Support for the efficacy of Tisseel would be provided if: (1) there were no significant differences in patient characteristics among the three groups; (b) there were no significant differences in surgical variables, such as rate of reoperation for bleeding and the use of blood products, between the groups II and III; (c) group II and group III significantly differed from group I, displaying reduced rates of reoperation for bleeding and decreased in the use of blood products; and (d) there was no trend towards improvement over time.

Materials and Methods

Three groups of patients were studied through a retrospective chart review. Group I consisted of 100 patients in whom no fibrin sealant was used during cardiac surgery, and these patients were consecutively operated on from 26 September 1988 to 26 February 1989. Group II was composed of the 100 patients immediately following this group and included consecutive patients operated on from 27 February 1989 to 10 July 1989. There were the first 100 patients in whom Tisseel fibrin sealant 5 cc in a spray form was used. Group III consisted of 100 patients in whom Tisseel fibrin sealant was used consecutively exactly 1 year later, from 27 February 1990 to 29 June 1990. Tisseel was used continuously from 27 February 1989 on all patients until the last patient of this study on 29 June 1990. The time-line (Fig. 1) illustrates these groups.

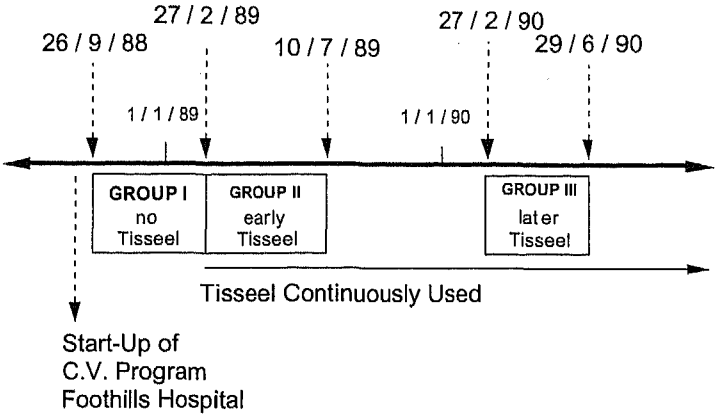

Fig. 1. Time line

The demographic characteristics of the three patient groups were very similar. The mean overall age was 62 years and 79 % were men. In groups I, II and III the corresponding figures were: 63.3 years, 75 % men (n = 96); 61.4 years and 83.3 % men (n = 96); and 61.8 years, 78.3 % men (n = 97). Of these 300 patients, 40 % were elective or planned, with the remaining 60 % being in the urgent/emergent category. They included 75 % with aortic coronary bypass surgery, 17 % valves, 8 % and combined bypass and valve. Six percent of the total were repeat operations or "redos" from other centres. Table 1 shows the types of surgery. Eleven patients were excluded because of lost records, intra-operative deaths, or surgery performed with cardiopulmonary bypass on stand-by only.

The general characteristics of these three patient populations compared were category of urgency of surgery and type of surgery. In the province of Alberta we have established four categories of urgency: elective or planned, urgent out-of-hospital (those who should receive heart surgery with 2 weeks, for example, a mildly symptomatic aortic stenosis), urgent in-hospital patients (those who cannot be discharged until they have surgery, such as those with unstable angina on a heparin drip), and emergency patients (those requiring surgery within 24 h of diagnosis). Surgical characteristics were also compared

Table 1. Type of surgery

	Overall Sample		Group I (no Tisseel)		Group II (early Tisseel)		Group III (late Tisseel)	
	n	%	n	%	n	%	n	%
Aortic coronary bypass surgery	217	75.09	71	73.96	78	81.25	68	70.1
Valve surgery	47	16.26	14	14.58	13	13.54	20	20.62
Combined bypass and valve surgery	25	8.65	11	11.46	5	5.21	9	9.28

between the three groups: degree of hypothermia with cardiopulmonary bypass, total time on cardiopulmonary bypass ("pump time"), and time of cardiac arrest for completion of operative procedure ("cross-clamp time"). We used moderate systemic hypothermia for all of the heart surgery in this study. Chest tube drainage was measured for the first postoperative 24 h and total drainage until all chest tubes, including mediastinal and pleural, were removed.

In addition, the transfusion rate between the three groups was compared by measuring preoperative hemoglobin and hemoglobin on the first and fifth days postoperatively. The difference was then calculated between preoperative and first day postoperative hemoglobin and the difference between preoperative hemoglobin and hemoglobin 5 days postoperatively. The differences between the three groups were compared as a marker of transfusion rate of the three groups. For example, if the difference between preoperative and 1 day postoperative levels in the group of patients without Tisseel was 10 g hemoglobin, and the same difference for the patients in groups II and III in whom Tisseel was used was 40 g hemoglobin, one could say that the first group of patients were relatively overtransfused compared to the latter two groups. We also measured hemoglobin at 5 days because by this time most of the edema from crystalloid transfusions at the time of heart surgery has been diuresed.

Parameters measured to study the efficacy of Tisseel in controlling bleeding included: resternotomy rate for bleeding, chest tube loss at 24 h and total, transfusions of blood products, and transfusion of individual blood products including units of packed cells, plasma, platelet concentrate, and cryoprecipitate. We also noted those patients in whom no blood products were used.

To determine whether Tisseel helped to improve the speed of operating, (i.e., taking less time for hemostasis), the interval during which hemostasis principally occurred was monitored, the interval from the patient's being taken off cardiopulmonary bypass until skin closure, is referred to as the "pump to finish time."

Means and standard deviations were calculated for each variable. Overall differences among Tisseel groups for each continuous variable of interest were evaluated by analysis of variance. Categorical variables were evaluated by the chi-square statistic. A conservative level for statistical significance, $p < 0.01$, was chosen, due to the retrospective nature of this study and the number of analyses conducted. Variables which demonstrated significant differences among the Tisseel groups were further analyzed through pairwise comparisons. Continuous variables were evaluated by independent t tests and categorical variables by chi-square.

Results

Table 2 shows the categories of the three groups relating urgency of operation and, interestingly, the trend in our institution has been to less and less electives and more patients in the urgent/emergent category. Only 20 % of the patients were elective in group III (late Tisseel) compared to 48.9 % in group I (no Tisseel; $p < 0.001$), and 52 % in group II (early Tisseel; $p < 0.001$).

Table 2. Category of urgency (percentages)

	Overall Sample	Group I (no Tisseel)	Group II (early Tisseel)	Group III (late Tisseel)
Elective	40	48.9	52	20.6
Urgent, out of hospital	9	10.4	2	12.4
Urgent, in hospital	40	29.1	39.6	52.6
Emergency	11	11.5	6.2	14.4

Distribution in I vs. that in III, $p < 0.001$; distribution in II vs. that in III, $p < 0.001$.

Surgical statistics compared included: hypothermia, pump time, and cross-clamp time (Table 3). The average temperature in group I was 30.14 °C, in group II 31.33 °C, and in group III 31.81 °C. Although the difference between group I and group II and that between group I and group III are statistically significant, we do not feel that the temperature difference of 1.19 ° (group I vs. group II) or 1.67 ° (group I vs group III) is clinically significant. Initially, time on the cardiopulmonary bypass or pump time was long; the group I average was 106.9 min. This time shortened in group II to 89.6 min and lengthened in group III to 109.1 min. The average pump time of group II was significantly different from that of group I ($p < 0.01$) and that of group III ($p < 0.001$); this is discussed below. The average cross-clamp time displayed a similar pattern of differences among the three groups. In group I (no Tisseel) the cross-clamp time was 58 min, in group II (early Tisseel) 53.9 min, and in group III (later Tisseel) 67.1 min. The only significant difference ($p < 0.001$) was between groups II and III (13.2 min longer for group III).

The differences between preoperative and 24 h postoperative hemoglobin levels were very similar among the three groups: group I, 41.9, group II, 48.3; and group III, 42.8. In each case the level was lower 24 hours postoperatively. There were no statistically significant differences between any pairs of hemoglobin differences. The values at 5 days postoperatively compared with the preoperative hemoglobin for the three groups were: group 1, 29.0 g; group II, 33.9 g; and group III, 37.6 g. In each case postoperative levels were lower than the preoperative values. The only significant difference between pairs of these differences was that between groups I and III ($p < 0.001$).

Table 3. Surgical variables

	Group I (no Tisseel)	Group II (early Tisseel)	Group III (late Tisseel)
Temperature (°C)*, **	30.14 ± 1.74	31.33 ± 2.47	31.80 ± 2.65
Pump time (min)***, ‡*	106.9 ± 40.7	89.6 ± 36.1	109.1 ± 44.0
Cross-time clamp (min)***	58 ± 23.9	53.9 ± 22.4	67.0 ± 28.7
Pump time to finish (min)*, **	74.88 ± 38.88	57.6 ± 24.48	56.8 ± 24.48

* I vs. II, $p < 0.001$; ** II vs. III, $p < 0.001$; *** II vs. III $p < 0.001$;
‡* I vs. II, $p < 0.01$.

Table 4. Chest tube drainage (cc)

	Group I (no Tisseel)	Group II (early Tisseel)	Group III (late Tisseel)
First 24 h*	1433.9	1095.1	855.2
Total*	1834.5	1288.5	1108.2

* I vs. III, $p < 0.001$.

Table 4 shows the chest tube drainage for the first postoperative 24 h and total drainage from all chest tubes, mediastinal and pleural. The only difference between the two groups that achieved statistical significance was that between group I and group III, both at 24 h and total.

Table 3 also shows the pump time to finish or the time taken when hemostasis occurs during surgery. In group I (no Tisseel) this time measured 74.8 min, in group II (early Tisseel) 57.6 min, and in group III 56.8 min. There was no statistical difference between groups II and III; however, both groups II and III had significantly shorter times than group I ($p < 0.001$).

The resternotomy rate for bleeding (Table 5) was significantly lower in both groups II and III than in group I. There was no statistical difference between groups II and III than in group I ($p < 0.001$, $p < 0.001$, respectively). The percentage of patients whose resternotomy was due to surgically caused bleeding was not significantly different for any comparison between the three groups.

Table 6 shows total transfusions and multiple- and single-unit transfusions for each of the three groups. The average number of transfusions per patient in group I was 23.7. This contrasts significantly with 10.3 in group II ($p < 0.001$) and with 13.2 in group III ($p < 0.01$). In terms of individual blood products there were no significant differences (Table 7); it was felt that the samples were too small to achieve significance. Types of units that one tends to order singly were therefore combined (units of packed cells and plasma), as were those which one tends to order in multiples (units of platelets and cryoprecipitate). There were significantly fewer units of blood products which are commonly used singly for patients in groups II and II than for those in group I ($p < 0.001$). A significant difference in the use of units ordered in multiples was found only in that between group I and group II ($p < 0.01$).

Table 5. Reoperation for bleeding

	Group I (no Tisseel)		Group II (early Tisseel)		Group III (late Tisseel)	
	n	%	*n*	%	*n*	%
Total*, **	21	21.8	7	7.29	5	5.15
Surgical cause	8	8.33	2	2.08	2	2.06
Nonsurgical cause	13	13.54	5	5.20	3	30.9

* I vs. II, $p < 0.01$; ** I vs. III, $p < 0.001$.

Table 6. Blood product use

	Group I (no Tisseel)	Group II (early Tisseel)	Group III (late Tisseel)
Total transfusions (units)*, 4*	23.69	10.34	13.18
Multiple-unit transfusions (units)**	12.51	5.08	7.67
Single-unit transfusions (units)*, ***	11.17	5.26	5.01
No blood products used (%)**, ***	10.41	33.33	38.14

* I vs. II, $p < 0.001$; ** I vs. II, $p < 0.01$; *** I vs. III, $p < 0.001$; 4* I vs. III, $p < 0.01$.

Table 7. Individual blood product use (units)

	Group I (no Tisseel)	Group II (early Tisseel)	Group III (late Tisseel)
Red cell concentrates	6.85	4.74	5.98
Fresh-frozen plasma	7.95	6.38	6.63
Platelet concentrate	13.46	12.39	16.07
Cryoprecipitate	16.93	11.86	14.63

Table 6 also shows those patients in whom no blood products were required. The two groups in which Tisseel was used (groups II and III) had significantly higher percentages of patients requiring no blood products (group II 33.33 %, group III 38.14 %) compared with group I (10.41 %).

Discussion

Fibrin sealant was first used in cardiovascular surgery by Spängler in 1976 [7]. Rousou et al. [8] clearly demonstrated the efficacy of fibrin sealant in their study; the success rate between fibrin sealant and conventional topical hemostatic agents was highly significant, at 92.6 % vs. 12.4 % ($p < 0.001$). Eleven centers were involved, and the protocol in ten of these specified that fibrin sealant should be applied after heparin reversal by protamine. In the 11th center the protocol allowed application of fibrin sealant to bleeding sites while the patient was still fully heparinized. In this setting fibrin sealant was extremely successful and achieved hemostasis in 40 of 41 bleeding episodes within 5 min. Our study also shows the effectiveness of Tisseel in a most conclusive way. The aspect which led us to believe that it was Tisseel that produced our significantly improved results was probably its immediate effect on the first few patients. There was not a gradual improvement in the reoperation rate for bleeding, blood product usage, or chest tube loss. The results were dramatic, and for this reason we continued to use Tisseel on every patient.

Many reports in the literature attest to the importance of fibrin sealants in hemostasis in cardiovascular operations. Borst et al. applied fibrin adhesive 413 times in a group of 340 patients undergoing extracorporeal circulation when-

ever conventional suturing appeared impossible, difficult, or dangerous – with a success rate of 95 % [9]. Spotnitz et al. [10] used fibrin glue in the form of a spray on 20 consecutive patients and compared chest tube outputs with 20 controls. This sealant, not a commercially prepared solution, resulted in reduction of perioperative hemorrhage from the anterior mediastinum ($p < 0.05$). Matthew et al. [11] the reported use of a single-donor fibrin sealant system in 689 thoracic and cardiovascular procedures over a 4-year period and found an excellent overall success rate (94 % effective) with a reduction in the leakage of air, blood, and fluid as well positioning of anatomical structures such as coronary bypass grafts.

This retrospective study of Tisseel fibrin sealant in patients undergoing open-heart surgery is unique in that this product for hemostasis was used consecutively in all patients. In most centers [6, 9, 11] Tisseel has been used in high-risk cases or in patients who subsequently develop coagulopathy during the operation. Also, only two surgeons were involved, and at the beginning of the program they actually assisted one another, lending uniformity to the surgical practice. The type of surgery performed was quite consistent, with a similar proportion of valves, bypasses, and combined procedures. The reoperation rate was low in this patient population compared with that at other centers, obviously because the program was just commencing. The primary cardiologist of these patients requiring reoperations was based at Foothills Hospital and had referred these patients for their first surgery before our unit was open. The one group characteristic that was significantly different was the higher proportion in group III undergoing urgent/emergent surgery (Table 2). Urgent/emergent patients have greater problems with bleeding than do planned or elective patients and may require more blood products. We were very interested to see that this group, which represented almost 80 % urgent/emergent, had the same significantly lower chest tube drainage, resternotomy rate for bleeding, and reduced total transfusions. Also, most significantly this group had the most patients who required no blood products at all. Both the cross-clamp time and total pump time were longest in group III. Again, this represents another possible indicator of the changing category from the more stable to the higher risk patient. However, from all the numbers demonstrated the bleeding problems in group III seem to be less than those in group I, whose patients had shorter cross-clamp and pump times. Therefore this demonstrates more conclusively the effectiveness of Tisseel.

The pump time to finish was significantly shorter in the two groups using Tisseel, and it therefore is likely that Tisseel did help speed the operation; however, not all factors were controlled, and since this was a retrospective study, there are undoubtedly other reasons for this quicker finish. However, the trend certainly suggests easier hemostasis with Tisseel.

The trend has been to accept lower postoperative hemoglobin levels because of the attendant risks of hemologically transmitted diseases. In the literature the chest tube drainage has remained relatively constant at approximately 100 ml; however, the total postoperative administration of packed red cells has decreased from more than 8 U to less than 3 U [12, 13]. Transfusion transmitted viral diseases are a most serious complication of cardiopulmonary

bypass – 27 % of individuals contracting acquired immunodeficiency syndrome related to transfusions are accounted for by cardiac surgery patients [13]. Although the human immunodeficiency virus seronegative blood has reduced this complication, it has not been completely eliminated in these patients [14]. In a stable patient population it is ideal to transfuse previously deposited autologous blood; however, in our patient population, especially with the 80 % urgent/emergent cases in the third group of patients, this was not possible. In our unit we have reserved such a practice for those patients undergoing planned procedures, such as atrial septal defect repairs or arrhythmia surgery. Intraoperatively all shed blood is reinfused at the time of surgery, either with the cardiotomy suction apparatus for heparinized blood or with the cell-saver for protamine-reversed heparinized blood and nonheparinized blood. We did not use autotransfusion postoperatively because we found that in the majority of patients it was not necessary, and that those who bled significant quantities had coagulopathies. Reinfusing such blood leads to transfusion of fibrinogen-split products, further compounding the existing coagulopathy.

We measured hemoglobin preoperatively and compared it with the postoperative value at 24 h and 5 days to ascertain whether the transfusion rate among patients in group I differed rates of patients in groups II and III. The hemoglobin level of all groups fell 43–48 g immediately after surgery, indicating a similar transfusion rate at this point in time. After 5 days there was no significant difference between groups I and II; however, there were slightly lower hemoglobin levels in group III than in group I ($p < 0.001$). Several explanations could account for this; it is possible, for example, that the rate of transfusion for days 1–5 was greater in our first group of patients. Our policy towards transfusion, as in many other centers [1], has changed in that lower hematocrit levels are being accepted. Four years ago patients would be transfused if their hemoglobin reached the middle 80s, and now our transfusion level occurs if it drops to the middle 70s, taking into account the patient's age and hemodynamic stability. However, in the operating room our transfusion rate has not changed over the years. For the most part, patients are transfused according to a lowest hematocrit level acceptable on cardiopulmonary bypass. On review of all the patients in addition to those in this study, it appears that this trend to less transfusion had occurred slowly and affects only the comparison between groups I and III, 5 days postoperatively. Perhaps transfusions occurring only at surgery and in the first 24 h would more accurately reflect the blood product usage and the effect of Tisseel. A second possibility is that the patients in group III were more vigorously diuresed. This is extremely likely because the intensivists who looked after our patients in the immediate postoperative period were reluctant to actively diurese the patients. The retrospective nature of this study precludes identifying the causative factor for this greater hemoglobin drop at day 5 in group III.

The chest tube drainage was certainly decreased in group II at both 24 h and in total. The drainage was even lower in group III; however, this reduction is significant only compared with group I. This could nevertheless be considered as part of a learning curve for a surgical unit. Regarding at the actual figures, although not achieving statistical significance (Table 5), clinically there

was quite a reduction in chest tube drainage (338.8 and 545.7 cc) between group II and group I at 24 h and in total drainage, respectively.

In terms of individual blood product use there was no significant reduction in any type of unit used when comparing all three groups (Table 7). The numbers are small, however, and may not represent a large enough sample to achieve statistical significance. Regarding total transfusions significantly fewer blood products were used in groups II and III than in group I. However, the difference between groups III and I was less significant ($p < 0.01$) than that between groups II and I ($p < 0.001$). This may relate to the more urgent/emergent cases in this group and longer cross-clamp and pump times, reflected in greater blood products needed. Units of blood products which one tends to order in multiples, that is units of platelets and units of cryoprecipitate, carry a higher risk of transmitting blood-borne diseases such as AIDS or hepatitis. A reduction in these types of units is more significant given a higher risk of exposure to blood-borne diseases. There were significantly fewer of these types of units ordered in group II ($p < 0.01$) and, although not statistically significant, still fewer by almost 5 U in group III ($p < 0.075$). When we compared the single unit blood products, that is those units of blood products ordered singly (packed cells and units of plasma), many fewer units were used in both groups in which Tisseel had been used ($p < 0.001$); again, this substantiates that a learning curve was not responsible for the improvment.

Perhaps the most desired result is to increase the number of patients requiring no blood products. No transfusions of any kind means no possibility of AIDS, hepatitis, or other transfusion-related diseases. In both groups using Tisseel there were significantly greater number of patients undergoing open-heart surgery with no blood products. This is especially important when considering the recent method of lyophilized steam treated at 60° for 10 h under 1190 MB, which eliminates both HIV and the hepatitis virus.

Resternotomy for bleeding after cardiac surgery should occur in fewer than 3% patients [15]. When patients undergo reoperation for excessive bleeding, more than half exhibit significant incomplete surgical hemostasis, that is, that which is corrected by reexploration [1]. In our patients (Table 5) the overall rate of surgical bleeding was 36% (12/33). Certainly the majority of patients in group I who required reoperation for bleeding were found to have a nonsurgical cause (13/21, 62%). In the 200 patients treated with Tisseel, although the percentage of patients with no surgical cause was the same (8/12, 66%), the absolute numbers were greatly reduced: 12 patients in the 200 compared with 21 in the first 100.

Summary

Our four criteria to support the efficacy of Tisseel are satisfied as follows: (a) All patient characteristics of the three groups were statistically similar except the increase in group III of patients undergoing urgent/emergent surgery. (b) Differences in surgical variables existed: pump and cross-clamp time were longest in group III; hemoglobin differences at day 5 were greater in group III.

(c) groups II and III differed from group I significantly in: pump to finish time, resternotomy rate for bleeding, total transfusions, transfusion of "singly" ordered units of packed cells and plasma, patients requiring no blood products, units ordered in multiples (cryoprecipitate and platelets) for group II, and chest tube drainage in group III. (d) Trends over time probably occurred in this population and were related to higher risk patients and possible changes in transfusion and diuresis practice postoperatively.

On balance, Tisseel fibrin sealant was very effective in reducing bleeding, reoperation for bleeding, and the requirement for transfusions in this group of cardiac surgical patients.

References

1. Woodman RC, Harker LA (1990) Bleeding complications associated with cardiopulmonary bypass. Blood 76 (9): 1680–1697
2. Kirklin JW, Barratt-Boyes BG (1988) Cardiac surgery morphology, diagnostic criteria, natural history, techniques, results, and indications part I, section III. Churchill Livingstone, Edinburgh, pp 158–159
3. McCarthy PM, Popovsky MA, Schaff HV et al (1988) Effect of blood conservation efforts in cardiac operations at the Mayo Clinic. Mayo Clin Proc 63: 225–229
4. Love TR, Hendren WG, O'Keefe DD, Daggett WM (1987) Transfusion of predonated autologous blood in elective cardiac surgery. Ann Thorac Surg 43: 508–512
5. Hans GB, Haverich A, Walterbusch G, Maatz W (1982) Fibrin adhesive: an important hemostatic adjunct in cardiovascular operations. J Thorac Cardiovasc Surg 84: 548–553
6. Rousou JA, Engelman RM, Breyer RH (1984) Fibrin glue: an effective hemostatic adjunct for nonsuturable intraoperative bleeding. Ann Thorac Surg 38 (4): 409–410
7. Spängler HP (1976) Gewebeklebung and lokale Blutstillung mit Fibrinogen, Thrombin und Blutgerinnungsfactor XIIL. Wien Klin Wochenschr 88 [Suppl 49]: 1–18
8. Rousou J, Levitsky S, Gonzalez-Lavin L, Cosgrove D, Magilligan D, Weldon C, Hiebert C, Hess P, Joyce L, Bergsland J, Gazzaniga A 1989 Randomized clinical trial of fibrin sealant in patients undergoing resternotomy or reoperation after cardiac operations. J Thorac Cardiovasc Surg 97: 194–203
9. Borst HG, Haverich A, Walterbusch G, Maatz W (1982) Fibrin adhesive: an important hemostatic adjunct in cardiovascular operations. J Thorac Cardiovasc Surg 84: 548–553
10. Spotnitz WD, Dalton S, Baker JW, Nolan SP (1987) Reduction of perioperative hemorrhage by anterior mediastinal spray application of fibrin glue during cardiac operations. Ann Thorac Surg 44: 529–531
11. Matthew TL, Spotnitz WD, Kron IL, Daniel TM, Tribble CG, Nolan SP (1990) Four years' experience with fibrin sealant in thoracic and cardiovascular surgery. Ann Thorac Surg 50: 40–44
12. Griffith LD, Billman GF, Daily PO, Lane TA (1989) Apparent coagulopathy caused by infusion of shed mediastinal blood and its prevention by washing of the infusate. Ann Thorac Surg 47: 400
13. Love TR, Hendre WG, O'Keefe DD, Daggett WM (1987) Transfusion of predonated autologous blood in elective cardiac surgery. Ann Thorac Surg 43: 508
14. Cohen ND, Munoz A, Reitz BA, Ness PK, Frazier OH, Yan DH, Lee H, Blattner W, Donohue JG, Nelson KE, Polk F (1989) Transmission of retroviruses by transfusion of screened blood in patients undergoing cardiac surgery. N Engl J Med 320: 1172

15. Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS (1991) Glenn's thoracic and cardiovascular surgery, 5th edn, vol II. Appleton and Lange, Englewood Fliffs, pp 1547–1559