



ORIGINAL ARTICLE

Is Platelet Rich Plasma (PRP) Injection in Sternotomy Wound Better for Healing and Pain Control?

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ABSTRACT

Background: Post-cardiac surgery with superficial and deep sternal wound infections (SWI & DSWI) raises morbidity and stay at hospital. In other surgical settings, autologous platelet-rich plasma (PRP), extracted from the patient's own blood, was used to facilitate effective wound healing. The aim of this work was to evaluate the usefulness of Platelet Rich Plasma (PRP) injection in sternotomy wound of patients undergoing cardiac surgical procedures. **Patient and methods:** A prospective study for patients underwent open heart surgery from June 2013 until June 2016 at Zagazig University. One hundred sixty patients were divided into two groups; group A: there is application of PRP before and after sternal closure in about 80 patients and group B: Sternotomy closure by ordinary manner without application of PRP in 80 patients. **Results:** Mean age was 54.32 ± 8.005 in group (A), ranged from 30 to 72 years and in group B, mean age was 55.21 ± 9.06 , ranged from 28 to 70 years. Follow-up of postoperative SSWI and DWSI showed that the use of PRP had no adverse reactions in our study. Also, the incidence of superficial and deep sternal wound infection from one month to more than 3 months in group A was reduced. Postoperative pain in group A had a significantly low incidence of moderate and severe pain in the period from one month to more than 3 months. **Conclusion:** Application of PRP in sternotomy wound in the treatment community was found to be quick, safe and significantly reduced postoperative infection levels and pain severity. **Key Words:** Platelet Rich Plasma, Sternotomy, Superficial and deep sternal wound infections

INTRODUCTION

One of the most severe complications associated with cardiovascular surgery is sternal wound infection (SWI). It is related to an increase in the hospitalization duration, hospital costs and the need for surgical re-intervention [1].

A clinical preventive approach has not yet been clearly established. The topical application of autologous platelet rich plasma (PRP) has been identified to promote earlier wound healing in a variety of settings [2].

PRP application is used to speed up the healing cascade through the action of elevated

cytokine concentrations produced during degranulation of the platelets. Examples of cytokines found to be present at concentrated levels in PRP are platelet derived growth factor (PDGF), epidermal growth factor (EGF), vascular endothelial growth factor and transforming growth factor beta (TGF- β) [3].

Several recent studies have shown the advantages of using PRP's topical treatment for enhanced postoperative outcomes following median sternotomy[4]. Nonetheless, the findings were contradictory and so far there is no conclusive evidence for using of PRP in DSWI prevention [5].

AIM OF THIS WORK

The aim of this study was to evaluate the usefulness of Platelet Rich Plasma (PRP) injection in sternotomy wound of patients undergoing cardiac surgical procedures.

PATIENTS AND METHODS

Prospective study for patients underwent open heart surgery from June 2013 until June 2016 at Zagazig University. We selected about 160 patients; divided into two groups: Group A: There is application of PRP before and after sternal closure in about 80 patients. Group B: Sternotomy closure by ordinary manner without application of PRP in 80 patients.

Preoperative preparation: All patients must stop antiplatelet for at least 5 days and not take any anti-inflammatory preparation.

Exclusion criteria: Long bypass time >120 minutes, renal or hepatic impairment, combined surgeries, HbA1c > 8, delayed sternal closure, pediatric patients, bleeding, emergency operation and low EF patients.

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Platelet rich plasma (PRP) preparation:

For preparation about 10 cm of PRP: Firstly, we drew about 100 cm blood from CVP after induction for anaesthesia. The drawn blood was put in sterile patient vacutainer (which contained sodium citrate which is an anticoagulant that does not affect in platelets).we used 50 sterile patient vaccination tube(each tube accommodates about 2 cm blood). Then, we started centrifuge 1500 round PM for 15 minutes. The content of tube was divided into 3 layers: basal layer: RBCs, mid layer: buffy coat, and upper layer: Plasma supernatant. By large bore cannulation, upper and mid layers of fluid were taken in the tube and put in plain vacutainer tube, then centrifuged for 5 minimal with 3500 rpm. It formed 2 layers; upper layer of plasma and basal layer of platelets. About 2/3 of plasma layer was

removed. Remnant of plasma layer and platelet layer were mixed to form PRP. We prepared about 10 cm PRP which was applied at sternal closed edges after closure, the sterum by wires and at site of jenter and exit the sternal exit.

Preoperative and intraoperative management:

All patients were prepared preoperatively in same manner. Firstly shaved on the night before operation. Then after induction of general anaesthesia and blood drawn for PRP preparation, the patients were draped and the skin was covered with adhesive plastic sheet. Standard full median stenrotomy and extracorporeal circulation were performed for all patients. Heparin was administered to achieve Act level over 500 second, at dosage of 300 Iu/kg. Systemic temperature left to be draft to around 32 degree. Intermittent antegrade warm cardioplegia of the blood is in all cases. Rewarming and weaning from CBP were performed after complete the surgery, then protamine were started to completely reverse heparin. Sternal closure was performed with eight stainless steel wires and then covered by two layers of reabsorbable suture to the muscle and subcutaneous tissues. Monocryl 3/0 was closed to skin.

Postoperative management:

Diagnosis of deep sternal wound infection:

DSWI diagnosis occurs when patients meet one or more of the following conditions, according to the Centers for Disease Control and Prevention Guideline [6]: An organism is removed from the culture of mediastinal tissue or fluid. During sternal reoperation evidences of mediastinitis are seen. Either of the following is present: chest pain, sternal instability, temperature above 38°C and either a purulent discharge from the mediastinum or an organism isolated from the blood culture or drainage culture of the mediastinal region [6].

SSWI are both skin and subcutaneous tissue infections only and sternum still healthy, require routine regular wound dressing, followed by antibiotic therapy and/or VAC and/or wire removal [6].

Degree of sternotomy pain:

We assessed the degree of pain based on Visual Analog Scale (VAS). VAS is a measure of psychometric response that can be used in questionnaires. This is a measuring device not specifically measured for individual characteristics or attitudes. When responding to a VAS object, respondents indicate their degree of agreement to a statement by indicating a location between two endpoints along a continuous line. The continuous or equivalent dimension of the scale separates it from discrete scales such as the Likert scale. There is proof that the visual scale has superior metric properties than the discrete scales [7].

All patients were transfer to ICU. Analgesic given in both group was opioid according to need for first 5 days postoperatively. In case of signs of wound infections, wound dressing was done regularly. Microbiological samples were sent. Degree of pain was detected in both groups. It was classified into minor (very mild, discomforting, and tolerable), moderate (distressing, very distressing, and intense), severe (very intense, utterly horrible, excruciating unbearable, unimaginable unspeakable).

Postoperative antibiotic prophylaxis is same in both groups for 7 days postoperatively. Usually patients were discharged after 7 days postoperatively with oral antibiotics. In case of isolation of organism from wound infection, antibiotic is given according to the culture. Postoperatively all patients were followed up in outpatient clinic at one week, one month and 3 months.

Statistical analysis

The SPSS software for Windows, version 23 (SPSS Inc., Chicago, IL) was used for the statistical analysis. Continuous variables are presented as mean \pm standard deviation and as absolute numbers or percentages are described as categorical variables. Prior to statistical analysis the data were tested for normality. The univariate analysis t -test was used to evaluate normally distributed continuous variables, while the Mann – Whitney U-test was used for those variables that were not normally distributed. Follow-up events that occur over time were defined

using the technique of the Kaplan Meier survival curve and associated tests of significance for the log rating. Comparisons where $P < 0.05$ is considered important.

RESULTS

Tables 1, showed that mean age was 54.32 ± 8.005 in group (A), ranged from 30 to 72 years and male to female ratio of 48:32. In group B, mean age was 55.21 ± 9.06 , ranged from 28 to 70 years, with male to female ratio of 45:35. The two classes were homogeneous for pre-operative and intraoperative risk factors, with no major statistical variations.

Table 2, Follow-up of postoperative sternal wound infection showed that PRP had no adverse reactions in our study and reduced the incidence of superficial sternal wound infection from one month to more than 3 months in group A. On the other hand, superficial sternal wound infection increased significantly in group B. Postoperative deep sternal wound infection was reduced with PRP from one week to more than 3 months in group A but in group B increased significantly. The hospital readmission rate for re-intervention (need VAC, secondary suture, pectoralis flap or omental flap) increased significantly postoperatively till the end of follow-up period in group B.

Table 3, Cultures of infected sternal wound showed that microorganisms associated with SWI and DSWI were mostly Staphylococcus strains.

Table 4, Regarding degree of pain depending on Visual Analogue Scale (VAS), follow-up of postoperative pain showed that the use of PRP significantly reduced the incidence of moderate and severe pain in the period from one month to more than 3 months in group A. on the other hand minor pain was the more prevalent degree in group A after one week to more than 3 months of follow-up period.

Table 5, Over the follow-up period from one week postoperative to more than 3 months, survival curves showed that patients in group A had less frequency of superficial (Figure 1) and deep sternal wound infections (Figure 2) significantly compared to group B (Log Rank $p=0.013$ and 0.047 respectively).

Table (1): Preoperative demographic, risk factors, intraoperative and postoperative risk factors in both groups

Parameters	Group A n=80	Group B n=80	P-value
Age Mean±SD	54.32±8.005	55.21±9.06	0.51
Gender (male)	48(60%)	45(56.25%)	0.73
BMI>30	5 (6.3%)	6 (7.5%)	0.75
Smoking	52 (65%)	56 (70%)	0.50
Dyslipidemia	31(38.3%)	33(41.3%)	0.74
DM	51(63.8%)	48(60%)	0.63
Hypertension	41(63.1%)	45(56.3%)	0.33
Chronic heart failure	8(10%)	12(15%)	0.34
History of endocarditis	3(3.8%)	4(5%)	0.69
COPD	7(8.8%)	6(7.5%)	0.66
History of CKD	4 (5%)	5(6.3%)	0.73
History of steroids	2(2.5%)	3(3.8%)	0.65
<u>Caradiac function</u>			
EF % Mean±SD	52.06±8.35	51.41±6.14	0.57
Albumin (g/dl) Mean±SD	4.06±0.53	3.97±0.39	0.28
Haemoglobin (g/dl) Mean±SD	11.72±2.04	11.36±3.19	0.057
TLC at admission Mean±SD	7.57±2.39	7.45±1.97	0.72
Platelets Mean±SD	190.82±56.11	189.03±59.68	0.83
<u>Opeation status</u>			
Elective	69(86.3%)	71(88.8%)	0.63
Non-elective	11(13.8%)	9(11.3%)	
Total length of stay (days) Mean±SD	10.37±2.21	10.15±2.27	0.75
Intraoperative and postoperative risk factors			
Isolated CABG with LIMA	46(57.5%)	52(65.0%)	0.33
Isolated valvular lesion	30 (37.5%)	25(31.25%)	0.32
CABG + Valves	4(5%)	3(3.75%)	0.69
Cardiopulmonary bypass time (CPB)>60minutes	12(15%)	13(16.3)	0.82
On-Pump (CPB)	60 (75%)	65 (70%)	0.47
Operative time (incision to closure)>300 minutes	14(17.5%)	12(15%)	0.66
Acute renal failure	3(3.8%)	5(6.3%)	0.46
Postoperative delirium	6(7.5%)	3(3.8%)	0.30
Respiratory failure	3(3.8%)	1(1.3%)	0.31
Hospital mortality	6(7.5%)	5(6.3%)	0.75

DM- diabetes mellitus; COPD – chronic obstructive pulmonary disease; CKD – chronic kidney disease; EF – ejection fraction; BMI – body mass index; CPB; cardiopulmonary bypass. TLC- total leucocytic count

CABG, coronary artery bypass graft; IMA, internal mammary artery, CPB; cardiopulmonary bypass

Table (2): Postoperative sternal wound infection

	Group A n=74	Group B n=75	P-value
After one week			
Superficial wound infection	3(4.10%)	6(8%)	0.31
Deep wound infection	-	4(5.30%)	0.044
Patients need secondary suture	-	3(4%)	0.038
After one month			
Superficial wound infection	1(1.4%)	12(16%)	0.002
Deep sternal wound infection	1(1.4%)	8(10.7%)	0.017
Patients need VAC	1(1.4%)	6(8%)	0.057
Patients need secondary suture	1(1.4%)	1(1.33%)	0.99
Patients need pectoralis flap	0	0	-
Patients need omental flap	0	0	-
After 3 months			
Superficial wound infection	0	3(4%)	0.002
Deep sternal wound infection	0	5(6.7%)	0.024
Patients need V A C	0	3(4%)	0.08
Patients need secondary suture	0	4(5.30%)	0.045
Patients need pectoralis flap	0	1(1.33%)	0.32
Patients need omental flap	0	5(6.7%)	0.025

Vacuum-assisted closure (VAC)

Table (3): Microorganisms associated with SWI and DSWI

Microorganisms	n=40 (%)
Coagulase-negative Staphylococcus	18 (45%)
Staphylococcus aureus (MSRA)	5(12.5%)
Klebsiella pneumoniae	4(10%)
Escherichia coli	5(12.5%)
Enterococcus faecalis	3(7.5%)
Enterobacter aerogenes	1(2.5%)
Enterococcus ssp	1(2.5%)
Pseudomonas aeruginosa	2(5%)
Acinetobacter ssp	1(2.5%)

Table (4): Degree of sternotomy pain

	Group A n=74	Group B n=75	P-value
After 1 week			
minor pain	54(73%)	10(13.3%)	<0.001
moderate pain	20(27%)	45(60%)	<0.001
severe pain	-	20(26.7%)	0.001
After 1month			
no pain	20(27%)	0	0.012
minor pain	48(64.8%)	22(29.40%)	0.011
moderate	5(6.8%)	34(45.30%)	0.002
severe pain	1(1.4%)	19(25.30%)	0.004
After 3month			
no pain	55(74.3%)	9(12%)	0.023
minor pain	12(16.2%)	40 (53.30%)	0.016
moderate	5(6.8%)	15(20%)	0.030
severe pain	1(1.4%)	11(14.7%)	0.002

Table (5): Survival functions for superficial sternal and deep wound infections in both groups

	Chi-Square	P-value
Superficial sternal infection		
Log Rank	6.219	0.013
Breslow (Generalized Wilcoxon)	5.066	0.024
Tarone-Ware	5.621	0.018
deep sternal infection		
Log Rank	3.928	0.047
Breslow (Generalized Wilcoxon)	4.02	0.051
Tarone-Ware	3.95	0.049

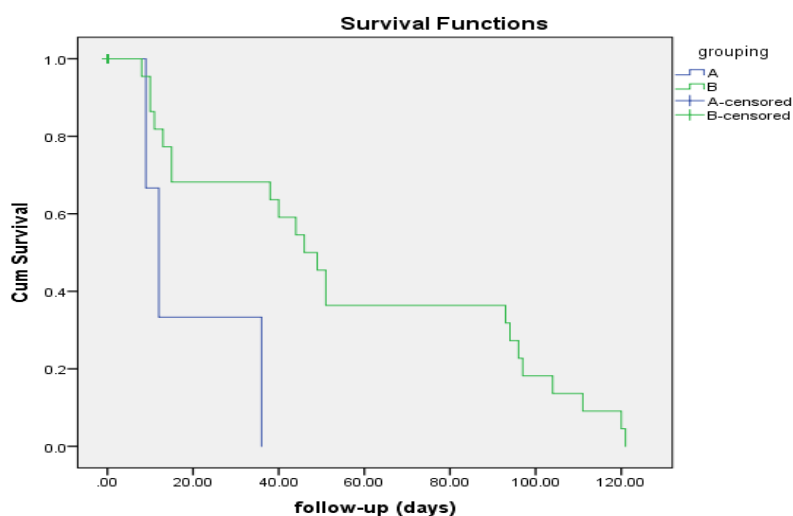


Figure (1): Superficial sternal infection in both groups

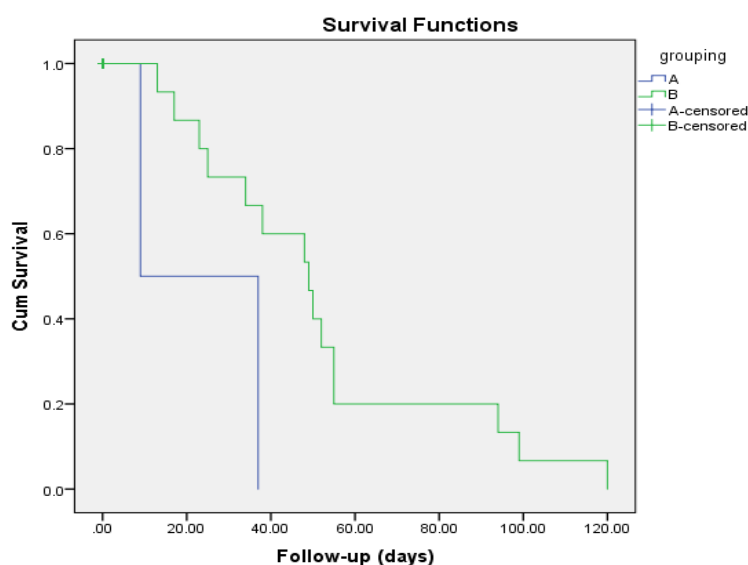


Figure (2): Deep sternal infection in both groups

DISCUSSION

Our study compared the incidence of superficial and deep sternal wound infections as well as pain severity after use of a PRP in patients who underwent cardiac surgical procedures. Follow-up of postoperative SSWI and DWSI showed that the use of PRP had no adverse reactions in our study. Also, the incidence of superficial and deep sternal wound infection from one month to more than 3 months in group A was reduced. Postoperative pain in group A had a significantly low incidence of moderate and severe pain in the period from one month to more than 3 months.

PRP, an autologous plasma fraction of the peripheral blood, is the easiest regenerative medicine technique that is now increasingly expanding to several medical fields, in particular many surgical specialties (such as plastic surgery, maxillofacial surgery and orthopedic surgery), primarily due to the ease of use and biosafety promoting human communication. [2,8,9].

Several authors have suggested application of PRP before wound closure in cardiac surgery with conflicting findings [10–12]. In the early 1990s the autologous PRP was suggested with strong clinical results in the treatment of DSWI [2].

Our results were consistent with the **Serraino et al.** study, which was conducted on 1093 consecutive patients undergoing cardiac surgery via median sternotomy, and the PRP was administered inside the sternotomy wound prior to closure in a community. They found that regular use of PRP could significantly reduce the incidence of either DSWI or SSWI without any adverse reaction to it [13].

The topical application of platelet gels has been similarly documented in a study by **Englert et al.** to decrease occurrence of sternal wound infections in patients with cardiac surgery [14].

Khalafi et al. also reported in a retrospective study of a successive series of patients undergoing a coronary artery bypass grafting procedure that platelet-rich injection and platelet-poor plasma significantly reduced incidence of infection of chest wounds [15].

Likewise, PRP's effects on the clinical outcome of patients receiving CABG were studied by **Buchwald et al.** PRP applied topically to chest and leg wounds appeared to have a beneficial effect on pain, swelling and blood loss [16].

Many publications may clarify the ability of PRP as a prophylactic tool to minimize the postoperative wound complications, in particular the risk of surgical site infection; it

is suspected that healing following median sternotomy is improved by growth factors released by the PRP. Activated platelets release unique growth factors during the inflammatory process of tissue regeneration, such as transforming growth factors-beta, endothelial vascular growth factor, and the epithelial growth factor. Such factors promote cell proliferation, migration, differentiation and synthesis of matrixes. These same factors can influence the metabolism of chondrocytes, chondrogenesis and enhance bone healing and regeneration [2]. In addition, the most common bacteria responsible for DSWI, *Staphylococcus aureus*, may be inhibited by the application of PRP [17].

Activated platelet concentrate has been promoted as a potential mode of immune response regulation, with platelet α -granules known to contain a family of cationic peptides which play a significant role in antimicrobial host defense [18].

In contrast to our findings, several studies didn't find that PRP in the sternal wound was associated with infection reduction; **Dorge et al.** [11] Concluded that the topical application of autologous PRP did not increase the incidence of DSWI in high-risk profile cardiac surgery patients. Regional use of autologous PRP in heart surgery patients with complete sternotomy at high risk for sternal complications did not minimize DSWI incidence.

Only, in patients undergoing cardiac surgery **Litmathe et al.** found no beneficial effect of PRP on wound healing. It can be argued, however, that a limited number of patients enrolled in both trials may have affected their findings [12].

The present research found that univariate analysis found that older ages, diabetes mellitus, chronic heart disease, and COPD patients were the statistically important risk factors for postoperative sternal wound infection. As with our findings, **Garey et al.** reported that older patients are at a higher risk of infection with sternal wounds. Older patients needing cardiothoracic surgery appear to have increased risk factors for infection. Many age-related comorbidities

increase the susceptibility of a patient to infections, while malnutrition tends to be the main cause of the worse immune function [19].

In some trials, age, COPD, and reoperation represented specific risk factors for SWI. Those variations can be due to disparities in the population [20-22].

Diez et al. have described COPD as an improvement in the risk of wound infection. COPD patients are more vulnerable to tissue hypoxaemia inducing surgical wound infection. Many of these patients require pre-and/or post-operative corticoid therapy which may facilitate the onset of infection [23].

Additionally, **McAlister et al.** have reported that diabetes patients are at a higher risk of sternal wound infection relative to other patients [24].

Diabetes has been linked to a higher SWI rate [25]. A broad retrospective study of diabetic patients undergoing cardiac surgery showed that hyperglycemia was an independent risk factor for death, duration of hospital stay, and infection levels and found that a continuous infusion of insulin minimized these risks [26].

In the current study, cultures of the infected sternal wound showed that microorganisms associated with SWI and DSWI were mostly *Staphylococcus* strains. Similarly, **Sjögren et al.** *Staphylococcus epidermidis* was confirmed to be one of the most common agents of poststernotomy mediastinitis; also, about 75% of *Staphylococcus epidermidis* strains are methicillin-resistant [27].

Staphylococcus aureus is the other major pathogen in Poststernotomy mediastinitis. The latter microorganism was gradually associated with the colonization of the nares of the patients. National Nosocomial Infection Surveillance System estimates that the MRSA prevalence in ICU patients with nosocomial infections increased from 30% in 1989 to 60% in 2005 and that MRSA was the causative microorganism in a third of DSWI patients [28].

CONCLUSION

In the treatment community, the application of PRP during surgical closure was found to be safe and significantly decreased levels of

postoperative infection and severity of pain. PRP is a safe, easy, and reproducible therapy that appears to provide both a clinical and a financial benefit for patients undergoing cardiac surgery sternotomy.

Limitations:

There is a number of limitations to this study including that it is a single-center study, small-sized sample.

Declaration of interest :

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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