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The impact of incisional negative pressure wound therapy on the wound healing process after midline sternotomy

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Abstract

Previous studies have reported that the use of incisional negative pressure wound therapy (INPWT) might reduce the incidence of wound infections, although its mechanism remains unknown. We designed a prospective study to explore the effects of INPWT on different stages of the wound healing process. After meeting the inclusion criteria, 108 patients were enrolled. Based on exclusion criteria four patients were excluded and 104 patients were randomised into two groups. INPWT was applied after primary closure of the midline sternotomy in the study group (n = 52), while conventional wound dressing was applied in the control group (n = 52). We documented the incidence of deep sternal wound infections and analysed the pre- and postoperative inflammatory biomarkers and scar size in both groups. No wound infections were observed in the study group compared with six cases (11.1%) in the control group, (P = .026). No significant differences were observed in the inflammatory biomarkers between the groups. Scar size was significantly smaller in the study group. We concluded that INPWT has less effect on the inflammatory phase and appears to have more effect on the proliferation phase through pronounced scar formation.

KEYWORDS
deep sternal wound infections, incisional negative pressure wound therapy, inflammatory biomarkers, proliferation phase, wound healing process

1 | INTRODUCTION

Survival rates after severe sternal wound infections are poor. Hence, there is many emphasis on preventing these infections, since survival is poor even after successful treatment.[1] In recent times, many measures have been introduced to prevent sternal wound infections, for example, preoperative nasal decontamination to prevent *Staphylococcus aureus* infection, application of gentamicin-coated sponge, vancomycin paste, administration of platelet enriched plasma, and incisional negative pressure wound therapy (INPWT).[2-10] Similar to all surgical wounds, healing of the midline sternotomy incision goes through the standard wound healing process; inflammation, proliferation, and remodelling phase. We hypothesised that vacuum application on the midline sternotomy incision would have an impact on the rate of complications by affecting the physiological process of wound healing. In this randomised prospective one centre study, we aimed to primarily evaluate the impact of INPWT on the wound healing process

after midline sternotomy. To elucidate the mechanism of the effect of INPWT, we examined the impact of INPWT on the post-wound inflammatory and proliferative phase.

2 | MATERIALS AND METHODS

The protocol of this prospective, randomised study conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in approval by the institutional human research review committee (approval No.: 071429-002/2016/OTIG). A total of 108 patients were consented and enrolled according to the study's inclusion criteria. Patients enrolled were those who were scheduled to undergo midline sternotomy and having at least one of the following risk factors: obesity (body mass index>30 Kg/m²); diabetes mellitus; peripheral vascular disease; and chronic obstructive pulmonary disease. Exclusion criteria involved lack of compliance for any reason, pre-operative screening positive for Methicillin-resistant *Staphylococcus aureus* (MRSA), and emergency surgery. Based on exclusion criteria four patients were excluded.

Subjects who met the inclusion criteria and gave their written consent (n = 104) were block randomised by an independent nurse who allocated them to either INPWT or control group (no INPWT). Figure 1 is a consort diagram showing patients' enrolment and randomisation into the INPWT and control groups.

Key Messages

- incisional negative pressure wound therapy (INPWT) has been reported to reduce the incidence of deep sternal wound infections; however, the mechanism is not well understood
- the aim of this prospective study was to explore the effect of INPWT on the different stages of the wound healing process. After enrolment of 104 patients who underwent midline sternotomy, we examined the changes in inflammatory biomarkers and scar size during the wound healing process
- the primary results appear to support the potential effect of INPWT on the proliferation phase of the wound healing process by reducing the scar size

2.1 | INPWT dressing

At the end of the surgical intervention and closure of the midline sternal incision, patients in the INPWT group received INPWT dressing (VivanoTec, Hartmann Ltd., Budapest, Hungary), while patients in the control group received conventional dry sterile gauze dressing (Figure 2).
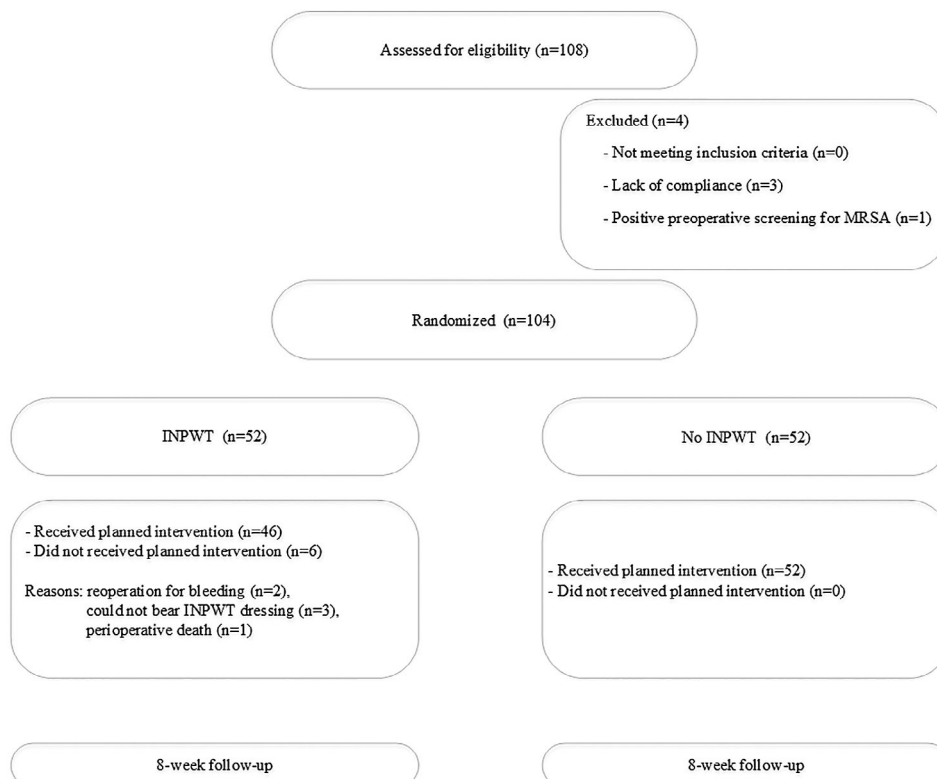

FIGURE 1 Consort diagram showing patients' enrolment and randomisation to the INPWT and control groups

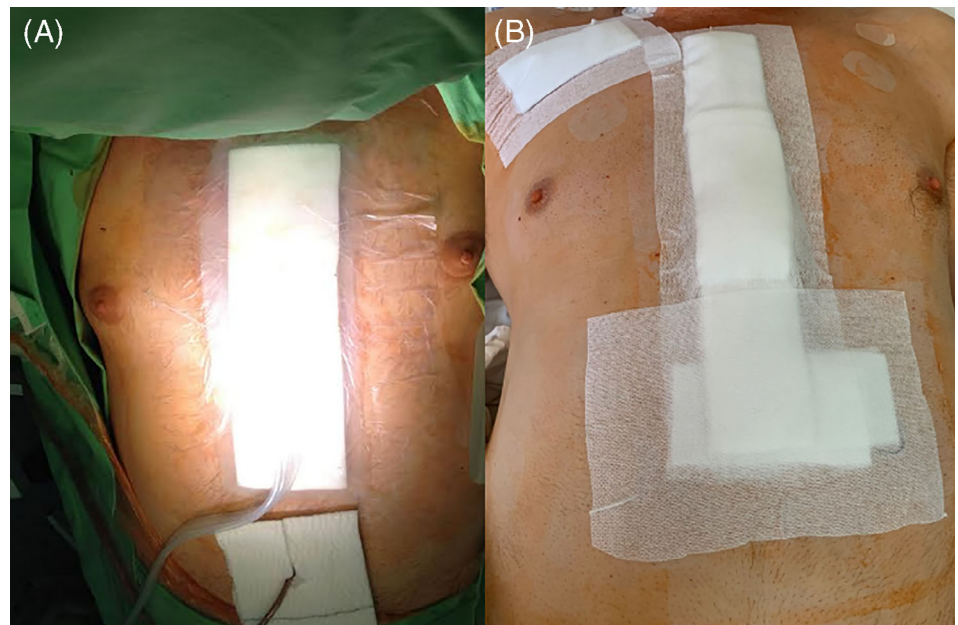**FIGURE 2** A, INPWT dressing, B, conventional gauze dressing

TABLE 1 Patients' characteristics of the INPWT and control groups

Baseline characteristics	INPWT group (n = 46, mean ± SD)	Control (n = 52, mean ± SD)	P-value
Age	67.26 ± 7.52	67.72 ± 7.29	.498
Sex (male, %)	71.4	74.1	.475
DM (%)	83.3	72.2	.149
PVD (%)	50.0	40.7	.243
Obesity (BMI ≥ 30Kg/m², %)	45.2	46.3	.541
COPD (%)	14.3	20.4	.438
CABG (%)	95.2	87.0	.171
Off pump CABG (%)	64.3	70.4	.339
IMA harvested (%)	73.8	68.5%	.369
RBCs transfusion (units)	1.5 ± 2.1	1.2 ± 2.1	.389
FFP (units)	0.27 ± 0.74	0.30 ± 0.92	.874
TCT (units)	0	0.30 ± 2.11	.392
Operation time (mean ± SD, minute)	158 ± 56	144 ± 52	.392
Intraoperative bleeding (mL)	488 ± 339	427 ± 269	.558
Postoperative bleeding (mL)	858 ± 433	867 ± 387	.917
Euroscore II	2.0 ± 1.7	1.8 ± 1.5	.111

Note: Bleeding from arrival at intensive care unit to the removal of chest drains.

Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; FFP, fresh frozen plasma; IMA, internal mammary artery; INPWT, incisional negative pressure wound therapy; PVD, peripheral vascular disease; RBCs, red blood cells; TCT, thrombocyte.
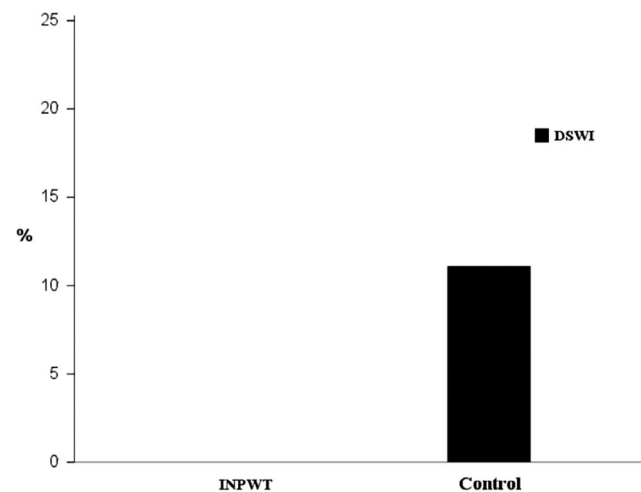

FIGURE 3 Incidence of DSWI in the INPWT group and control (no INPWT) groups

INPWT dressing consisted of a silicone net, polyvinyl alcohol-soaked white sponge, airtight hydrophil film, and vacuum generating unit. The dressing was connected to the vacuum generator by a two-line port. The vacuum was set to −125 mm Hg.

2.2 | Study course

All patients were treated according to the standard care at our institution. Preoperative preparation, sternal opening, and closure, as well as perioperative antibiotic prophylaxis, were standard for all patients enrolled in the study. INPWT treatment was continued for 5 days

postoperatively. To explore the potential impact of INPWT on the inflammatory phase of the post-wound healing process, we analysed three inflammatory bio-markers: C-reactive protein (CRP), mean platelet volume (MPV), and platelet distribution width (PDW) at four different time points, preoperatively and on the first, third, and sixth postoperative day. Evaluation of scar formation was performed by two-dimension (2D) ultrasound imaging (Esaote MyLab™ Twice). Two parameters were accurately measured: the distance between the sk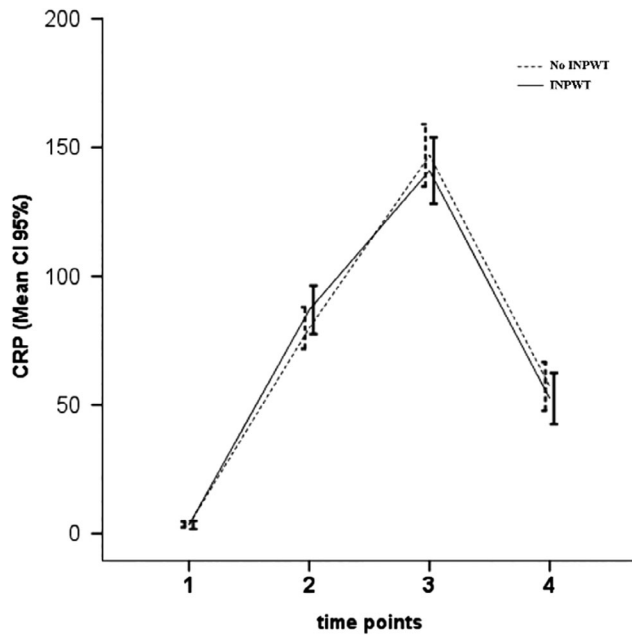in and sternum at the level of the fourth intercostal space denoted as C-S/0 (preoperative cutis to sternum distance) and the distance between the right and left pectoral muscle edges at the same level, denoted as P-P/0 (preoperative pectoral to pectoral distance). These parameters were measured again in the eighth postoperative week and denoted as C-S/1, and P-P/1, respectively. We assumed P-P/0 to be zero in all preoperative cases, as the pectoral muscles had not been incised yet.

Based on the Centre for Disease Control/National Healthcare Safety Network criteria,[11] deep sternal wound infection (DSWI) was defined if the infection involved at least the pectoral muscle fascia or deeper tissues in the incision, and the patient had at least one of the following: purulent drainage, organism isolated by culture-based microbiology testing, and signs of deep infection detected on gross anatomical or imaging test.

The primary outcome of this study was the occurrence of DSWI, change in inflammatory biomarkers, and the degree of scar retraction detected during 2D- ultrasound analysis.

2.3 | Statistical analysis

Study data were collected and analysed using the SPSS for Windows version 20.0 (IBM Corp., Armonk, New York). All data were presented as percentage, mean ± SD, or median with interquartile renge (IQR) in the case of non-normal distribution. For comparison of the basic data, the chi-squared test and Student's test were used. Continuous variables were checked for normal distribution by the Kolmogorov–Smirnov test and for homogeneity of variances with the Levene's test. If the results proved significant, Mann–Whitney U test was used consecutively. For comparison of the impact of INPWT on inflammatory biomarkers or ultrasound parameters of the scar, general linear model repeated measures analysis of variance (ANOVA) test was

FIGURE 4 C-reactive protein (CRP) test results (mg/dl) in the INPWT and control groups at the measurement time points. 1. prior to surgery, 2. first postoperative day, 3. third postoperative day, 4. sixth postoperative day. GLM Repeated Measures between-subject effects (F: 0.006, $P = .937$)

TABLE 2 Blood test results at the measurement time points in the IPWT and control groups

	1.	2.	3.	4.	F; P^a
CRP INPWT control	3.5 ± 5.1 3.4 ± 4.1	84.9 ± 29.3 80.0 ± 28.2	141.0 ± 40.1 142.8 ± 37.6	53.7 ± 32.9 55.7 ± 33.5	0.006; .937
PC INPWT control	228.2 ± 70.0 225.6 ± 58.9	193.5 ± 69.8 193.6 ± 62.5	177.4 ± 65.1 183.4 ± 64.0	263.0 ± 84.6 267.4 ± 97.3	0.021; .885
MPV INPWT control	8.6 ± 1.5 8.4 ± 1.3	10.2 ± 1.5 10.2 ± 1.2	9.7 ± 1.9 9.3 ± 1.5	7.9 ± 1.9 8.2 ± 1.6	0.181; .672
PDW INPWT control	16.0 ± 1.5 16.3 ± 1.1	16.0 ± 1.0 15.9 ± 0.8	15.9 ± 1.1 16.0 ± −1.2	16.1 ± 0.9 16.6 ± 3.5	1.374; .244

Note: 1. prior to surgery, 2. on the day 1 after surgery, 3. on the day 3 after surgery, 4. on the day 6 after surgery, (GLM Repeated Measures).
Abbreviations: CRP, C-reactive protein; MPV, mean platelet volume; PC, platelet count; PDW, platelet distribution width.
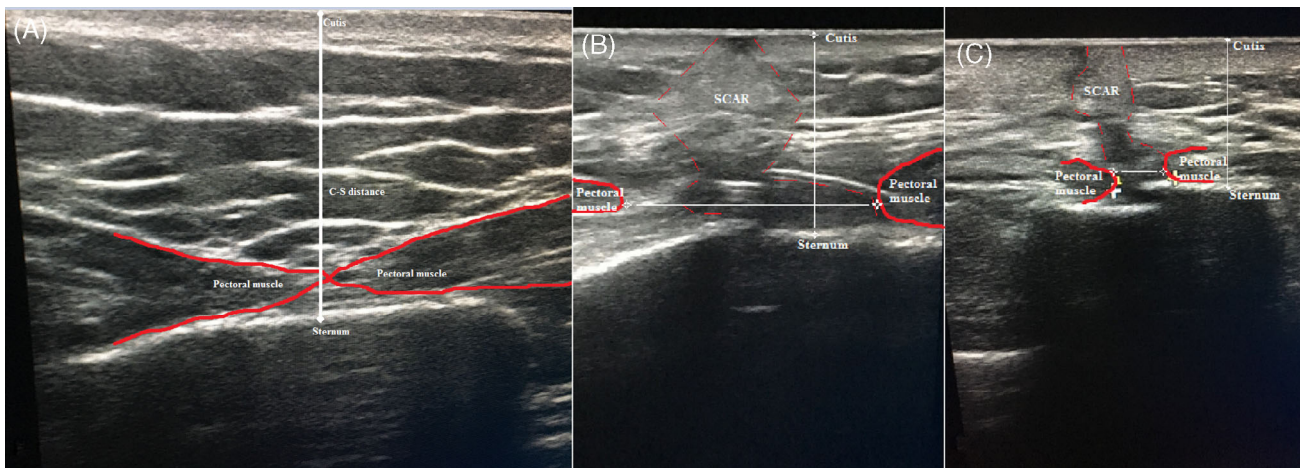[a]Test of between-subject effects.

FIGURE 5 Two-dimensional ultrasound imaging of scar before skin incision, A, and in the post-wound eighth week in the control, B, and INPWT, C, groups
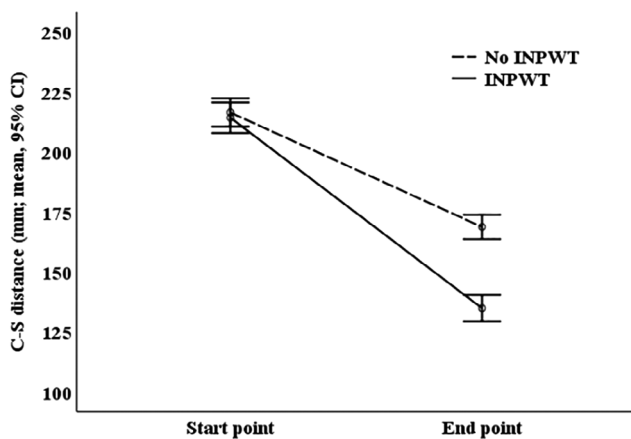

FIGURE 6 C-S distance in the control and INPWT groups. GLM Repeated Measures between-subject effects (F: 28.02, $P < .001$)
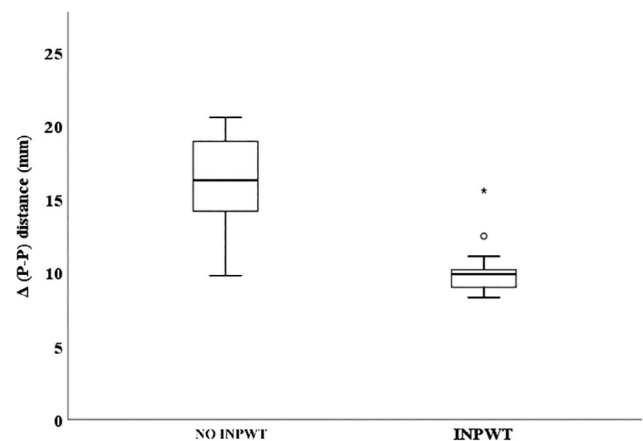

FIGURE 7 P-P distance changes in the control and INPWT groups. Boxplot (Mann–Whitney U test $P < .001$)

performed using "groups" as between-subject factor and "time" as a within-subject factor. To analyse the potential violation of the multivariate approach assumption, homogeneity analysis (Box's test), equality test of variance, and the sphericity test of the covariance matrix (Mauchly's test) were used. When the variance assumption of homogeneity or equality was not met, the Kruskal-Wallis test, in case of sphericity assumption violation, Greenhouse–Geisser correction was made. If a significant difference between the groups was detected, a Bonferroni *post hoc* test was performed to assess the differences at individual time points. $P < .05$ was considered statistically significant.

3 | RESULTS

No significant differences were detected in the patients' baseline characteristics between the groups (Table 1).

3.1 | Incidence of DSWI

Deep sternal wound infections occurred in 6.3% of the study population. No DSWI occurred in the INPWT group compared with six cases (11.1%) in the control group, ($P = .026$) (Figure 3).

3.2 | Impact of INPWT on inflammatory biomarkers

During the study course, no statistically significant difference was observed in CRP kinetics between the INPWT and the control group as shown in Figure 4.

Similarly, there were no statistically significant differences considering the platelet count, PDW, or MPV between the groups, (Table 2).

	Time point	DSWI (mean ± SD)	no DSWI (mean ± SD)	F	P
C-S	0	231 ± 28	214 ± 20	6.162	.015
	1	169 ± 30	152 ± 24		
Covariants					
Gender				2.215	.141
Age				1.862	.176
Obesity				20.38	<.001
DM				0.108	.743
COPD				0.988	.323
PVD				0.155	.695
CABG				2.499	.118
IMA				0.236	.629
RBCs transfusion				0.176	.676

TABLE 3 Results of GLM repeated measures of C-S in patients who developed DSWI (between-subject effect). Risk factors of DSWI were included in the analysis as covariants

Abbreviations: 0, prior to surgery; 1, 8 weeks after surgery; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; C-S, distance between the skin and sternum; DM, diabetes mellitus; DSWI, deep sternal wound infection; IMA, internal mammary artery; PVD, peripheral vascular disease; RBCs, red blood cells.

TABLE 4 Results of GLM repeated measures of P-P distance in patients who developed DSWI (between-subject effect)

	Time point	DSWI (mean ± SD)	DSWI (mean ± SD)	F	P
P-P distance	0[c]	0	0	4825	.031
	1[d]	17 ± 2.7	13 ± 3.9		
Covariants					
Gender				0.380	.539
Age				0.025	.875
Obesity				0.351	.555
DM				0.462	.499
COPD				3.053	.085
PVD				0.311	.579
CABG				1.922	.170
IMA				0.752	.389
RBCs transfusion				0.092	.763

Note: Risk factors of DSWI were included in the analysis as covariants.

Abbreviations: 0, prior to surgery; 1, 8 weeks after surgery; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; DSWI, deep sternal wound infection; IMA, internal mammary artery; P-P, distance between the right and the left pectoral muscle edges; PVD, peripheral vascular disease; RBCs, red blood cells.

3.3 | Impact of INPWT on the proliferation phase (scar formation)

Data obtained from two-dimensional ultrasound scar imaging (Figure 5) were analysed using general linear model (GLM) Repeated Measures. C-S and P-P parameters, given in mm-s, were significantly smaller in the INPWT group, $P < .001$ and $P < .001$, respectively, Figures 6 and 7.

Comparing the scar parameters in patients who suffered DSWI with those who did not, it was seen that C-S and P-P were significantly higher in the DSWI group.

Investigating the impact of risk factors of DSWI as covariants in the statistical model (GLM Repeated Measures), only obesity seemed to have a significant impact on the C-S distance (Tables 3 and 4).

4 | DISCUSSION

Deep sternal wound infections have been known to have a negative impact on morbidity, mortality, in-hospital treatment costs, and long-term survival.[12,13] Hence, it is

important to prevent these complications. There have been many efforts to prevent DSWI. However, a combination of different strategies might be more useful than adhering to a single preventive measure.

The beneficial effect of INPWT in reducing the rates of postoperative sternal wound complications was reported in many studies, while some studies demonstrated no benefit for the use of INPWT.[10,14] Our study results are in accordance with studies that reported a beneficial effect of INPWT, as no DSWI was documented in the INPWT group during the 8-week study period.

Although many risk factors for DSWI have been reported,[15,16] we were unable to incorporate all of them in this study. In the inclusion criteria, we considered only four main risk factors (DM, obesity, COPD, and PVD).

The mechanism of INPWT in reducing the rates of sternal wound infections is poorly understood. Analysis of the inflammatory biomarkers involved in this study showed no significant differences between the two groups throughout the inflammation phase. There could be two reasons for this; the first being that the effect of INPWT only impacted the local processes in the wound area and has no significant impact on the systemic inflammatory response. Another reason might be that INPWT might act through other inflammatory mediators, which were not included in our study. The correlation between INPWT and other inflammatory biomarkers might be a topic for further research.

Scar formation is an indicator of the repair process in the proliferation phase, which eventually leads to wound healing. Scar tissue is rich in collagen, predominantly type I. During the repair mechanisms, the pattern of collagen appearance in the scar tissue is usually less organised.[17]

Some prior studies had applied ultrasound imaging to evaluate the thickness and homogeneity of the uterine scar tissue after caesarean section.[18-20] In our study, the magnitude of the scar was analysed by 2D ultrasound imaging. Changes in wound contraction and organisation of the scar tissue between the INPWT and no INPWT groups were remarkable during the ultrasound analysis. Wound contraction was reflected by shorter distances between the incised pectoral muscle edges (P-P distance), and between the skin to the sternum (C-S distance), compared with preoperatively measured distance values. P-P0 was the distance between the pectoral muscle edges before the surgical incision, and it was assumed to be 0 in all cases. During the surgical incision, the pectoral muscles were incised in the midline. Due to the muscle tone, the edges of the right and left pectoral muscles move away from each other. At the end of the wound healing process, the space between the pectoral muscle edges was filled with scar tissue. P-P1 is the width of the scar tissue formed between the pectoral muscle edges after 8 weeks from the skin incision. Based on P-P and C-S measurements, a smaller scar was documented in the INPWT group of our study. P-P and C-S distance values were smaller in patients who had an uneventful wound healing process, compared with those who developed DSWI. This indicates that a smaller scar induced by INPWT can attribute to better wound healing with better cosmetic appearance and fewer wound complications.

The first limitation of this study is that it was a single-centre with a small sample size. The second limitation is the use of 2D US; 3D US evaluation might provide more accurate measurements of the scar volume. A multicenter study with a larger patient sample is necessary to further validate the results of this study.

5 | CONCLUSION

INPWT after median sternotomy reduced the incidence of postoperative sternal wound infections in our study. Although INPWT seems to have no impact on the inflammation phase, greater scar retraction indicates that it might facilitate earlier stimulation of the proliferation phase during the healing process of sternotomy wounds.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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