A Novel Absorbable Stapler Provides Patient-Reported Outcomes and Cost-Effectiveness Noninferior to Subcuticular Skin Closure: A Prospective, Single-Blind, Randomized Clinical Trial

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Background: Deep dermal suturing is critical for scar quality outcomes. The authors evaluated a new, fast medical device for dermal suturing, with the hypothesis of noninferiority with regard to clinical scar and cost-effectiveness.
Methods: A prospective, patient-blind, randomized, multicenter noninferiority study in 26 French hospitals was conducted. Patients were randomized 1:1 to suturing with conventional thread or a semiautomatic stapler. The Patient Scar Assessment Scale was rated at 3 months for primary endpoint effectiveness. Secondary endpoints were cost-effectiveness of the two suturing methods, prevalence of complications, suturing/operating time, Observer Scar Assessment Scale and Patient Scar Assessment Scale score, scar aesthetic quality 18 months after surgery, and occupational exposure to blood during surgery.
Results: Six hundred sixty-four patients were enrolled, 660 were randomized, and 649 constituted the full analysis (stapler arm, $n = 324$; needle arm, $n = 325$). Primary endpoint Patient Scar Assessment Scale score in the stapler arm was not inferior to that in the needle arm at 3 months or after 18 months. The mean operating time was 180 minutes in the stapler arm and 179 minutes in the needle arm (p = not significant). The mean suturing time was significantly lower in the stapler arm ($p < 0.001$). There were seven occupational exposures to blood in the needle arm and one in the stapler arm. The two arms did not differ significantly in terms of complications ($p = 0.41$). The additional cost of using the device was €51.57 for the complete-case population.
Conclusion: Wound healing outcome was no worse than with conventional suturing using a semiautomatic stapler and associated with less occupational exposure to blood. (*Plast. Reconstr. Surg.* 146: 777e, 2020.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, I.

Open surgery remains frequent and requires skin closure time. The time spent specifically on preparing and implementing sutures can account for more than one-third of the whole surgical procedure.

At present, deep dermal suturing is usually achieved by applying absorbable suture with a steel needle. Over the past 5 years, the introduction of new semiautomatic stapling technology (Insorb; Incisive Surgical, Inc., Plymouth, Mich.)

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has significantly reduced the closure time in this context. The staples are made out of a lactic acid/glycolic acid copolymer.[1] The staples are U-shaped with a hook at each end inserted with grip pressure; no needle handling is required. Composition and shape are part of its expected effectiveness. A cartridge of 30 staples is sufficient for the closure of a 20- to 30-cm incision. Complete hydrolytic resorption of the suture is observed 90 to 120 days after surgery.

The stapler has been prospectively assessed in several randomized, controlled preclinical and clinical trials in different contexts: hip replacement, kidney transplantation, and breast surgery. The trials' results have highlighted the technique's safety and good wound healing outcomes relative to conventional suturing.[2–4] Clinical and histologic scar assessments have evidenced equal or even better outcomes than those obtained with conventional sutures.[5,6] With regard to time savings, the main study published to date showed that the use of the stapler was associated with a 10-minute time saving per patient (average incision, 13 cm).[6] The closure time was three-fold shorter with the stapler than with a conventional technique. Thus, a U.S. study that assumed operating room production costs of $25 per minute found a production cost saving of $16 per centimeter for subcuticular suturing with this stapler, resulting in a mean total saving of $225 per patient with a small incision. The patient's level of satisfaction regarding the aesthetic outcome was greater with the new device.[4,5,7] Lastly, the scar's aesthetic qualities (Vancouver Scar Scale[8,9]) were similar to or better than those associated with conventional sutures.[5,6] The stapler became available in France in 2009; several pilot studies have confirmed the device's safety, ease of handling, and associated time savings.[10]

Despite these demonstrations of the device's safety and efficacy, several important questions have not been addressed. Challenges are not only about time. First, could the use of a semiautomatic stapler reduce the frequency with which infectious viruses (e.g., human immunodeficiency and hepatitis virus) are transmitted from patients to health care professionals? This issue may justify the use of a potentially safer stapler irrespective of the incision length.

Second, is the new stapler cost-effective? This parameter has not previously been assessed; the supposed cost savings associated with the subcuticular stapler in a North American study were based on assumed (rather than assessed) hospital costs.[6] Thus, the present prospective, multicenter, randomized, controlled trial in France was designed to confirm the device's effectiveness as the primary endpoint, in addition to its safety (for both the surgeon and the patient), tolerability, time savings (the overall operating time and the duration of anesthesia), direct patient benefits, and its cost-effectiveness relative to conventional suturing.

PATIENTS AND METHODS

We performed a prospective, patient single-blind, randomized, two-arm, parallel-group, multicenter, noninferiority trial. The two arms were not statistically different regarding comorbidities (70.4 percent in the device arm and 69.8 percent in the needle arm; p = not significant). The study's primary objective was to demonstrate that the deep dermal closure using an absorbable stapler is no less tolerable that the closure obtained with absorbable suture and a needle, defined by the reduced inferiority of the Patient Scar Assessment Scale score at 3 months. Other objectives included safety and cost-effectiveness in 26 university hospitals in France. The trial compared the absorbable subcuticular stapler with a standard treatment (i.e., absorbable polyglecaprone monofilament suture) (Monocryl; Ethicon, Inc., Cornelia, Ga.) with a steel needle.

The main inclusion criteria were as follows: patients aged 18 to 75 years; elective surgery for abdominoplasty, cervicotomy, or suprapubic surgery; a rectilinear or curvilinear open surgical approach at least 10 cm in length; an Eastern Cooperative Oncology Group Performance Status score of 0 or 1; and coverage by French health insurance. The study's exclusion criteria included surgical approaches requiring sinuous or very angular incisions (for which the stapler is not recommended); a history of intolerance to the devices or medications used; long-term treatment with corticosteroids, immunosuppressive agents, or medications that potentially interfere with wound healing; previous, ongoing, or anticipated skin infections; dermatologic diseases; previous local radiotherapy or ongoing treatment with a cytotoxic agent; pregnancy; and legal guardianship.

All participants provided informed consent before randomization. The protocol was approved by the ethics committee, and the study was conducted in accordance with the tenets of the Declaration of Helsinki, the International Conference Guideline for Good Clinical Practice, and European Clinical Trials Directive 2001/20/EC and Good Clinical Practice Directive 2005/28/EC.

The total study duration was 2.5 years, with a 1-year enrollment period and an 18-month follow-up period.

Endpoints

The primary endpoint was the total Patient Scar Assessment Scale score rated by the patient 3 months after surgery. This scale includes two symptom-related items (pain and itching) and four aesthetic items (color, stiffness, thickness, and regularity) ranging from 0 ("no complaints" or "normal skin") to 10 ("worst imaginable" or "very different"). The total Patient Scar Assessment Scale score is calculated by summing the six item scores and thus ranges from 6 (best) to 60 (worst).

The secondary endpoints were the incremental cost-effectiveness ratio (comparing the two types of sutures over a 3-month period); the prevalence of complications on day 8 after surgery (scar failure or infection); the anesthesia, suturing, and operating time; the Patient Scar Assessment Scale score 18 months after surgery; the total Observer Scar Assessment Scale score 18 months after surgery (rated by a surgeon who had not operated on the considered patient); the scar's aesthetic quality (scored on a 0 to 10 visual analogue scale) 18 months after surgery, according to the patient and surgeon); and occupational exposure to blood during surgery.

Randomization

After inclusion, the patient's randomization number and treatment arm were assigned by means of a Web-based randomization service (Capture System; Ennov Clinical, Paris, France). Block randomization was stratified by the type of department: ear, nose, and throat; gynecology; or plastic surgery.

Data Collection

At the time of surgery, any occurrences of occupational exposure to blood were recorded. One week after surgery, the investigator noted the scar's aspect/infections. The time interval between surgery and suture removal, any concomitant treatments, and the occurrence of complications were recorded until 18 months. Similar clinical examinations were performed 3, 12, and 18 months after surgery. If revision surgery was required at any time, a pathologic assessment of the scar was performed.

Cost-Effectiveness Analysis

We assessed the incremental cost-effectiveness ratio for the stapler versus conventional thread from a societal perspective and over a 3-month period. The incremental cost-effectiveness ratio was defined with regard to the primary criterion (the Patient Scar Assessment Scale score), as follows: (costs in the stapler arm – costs in the needle arm)/−(total Patient Scar Assessment Scale score in the stapler arm – total Patient Scar Assessment Scale score in the needle arm).

The cost-effectiveness study was conducted on both the complete-case and full analysis set populations.[11] Next, simple imputation (using the corresponding arm's mean and worst values, respectively) was used to interpolate the missing Patient Scar Assessment Scale scores and health care resource consumption data in the full analysis set.

The consumption of health care resources required for subcuticular suturing and the potential management of any complications up to 3 months after surgery were recorded prospectively. To precisely estimate the production cost of closure time, we performed a microcosting analysis in the operating room for a subsample of 80 patients; this involved rating the time spent by the health care professionals and the use of medical devices. The patient diary was used to rate resource consumption (medical consultations, drugs, laboratory analyses, radiographic examination) during the 3-month follow-up period. Lastly, we asked an expert board to estimate the expected consumption of health care resources in the event of occupational exposure to blood. Cost estimates for occupational exposure to blood were also based on the available French data for the estimated mean overall seroconversion rate (23.05 percent) following percutaneous exposure to seropositive blood containing at least one of the following viruses (hepatitis B virus, 2 to 40 percent in the absence of vaccination or immunization; hepatitis C virus, 0.5 to 3 percent; human immunodeficiency virus, 0.3 percent)[12] and the cost of treatment of seroconversion in France.[13] On this basis, the cost estimate was €664.04 per person for a 3-month period.

The unit monetary value of the resources consumed was determined using data from the coordinating investigator's hospital (e.g., staff salaries, device purchase prices) and the French national survey of hospital costs (https://www.atih.sante.fr/information-sur-les-couts/etudes-nationales-de-couts-presentation-et-recrutement) for its national insurance system. Resource costs were adjusted to 2014 euro prices (Table 1).

Given our focus on the cost difference, general hospital administration and logistics costs were excluded from our evaluation of the total cost of

Table 1. Resource Costs for Suturing*

Resources	Sources (2014)	Unit Cost
Health care professionals	Mean salary costs in two university hospitals	€3.18/min†
Materials	Hospital purchase cost	
Thread per unit		€3.30
Staple cartridges (2 × 30 staples)		€64.03
Consumables and drugs	Purchase cost	€0.13/min
Medical examination at 3 mo	Based on the French national health insurance system's tariffs	
General practitioner		€23
Specialist physician		€37‡
Consultation at the emergency department		€48.13
Laboratory assessments		€0.27

*In 2014 euros, for France.
†Given that no significant interarm difference was observed in the microcosting estimates of health care professional cost per minute, a single value was presented.
‡Mean value for various specialists according to the French national health insurance system's tariffs.

suturing. The total cost of subcuticular suture was estimated from the time of surgery up until the 3-month follow-up visit. The microcosting study of 80 patients provided an estimation of operating room costs of €3.18/ per minute (Table 1).

The per-patient mean ± SD, median, and interquartile range costs were reported for the suture arm and over a 3-month period. The 95 percent confidence intervals of the differences in per-patient total costs between the two arms were estimated by using the nonparametric bootstrap resampling technique.

Sample Size Calculation

We hypothesized that the Patient Scar Assessment Scale score should be similar in the two arms, with a standard deviation of 15 in both. The upper 95 percent confidence limit was compared with the noninferiority boundary for the standard technique in a unilateral test ($\alpha = 0.025$, $1 - \beta = 10$ percent). According to these hypotheses, the total number of patients required was 594. With an anticipated loss-to-follow-up rate of 10 percent, we sought to recruit 660 patients.

Statistical Analysis

We performed a per-protocol and a modified intent-to-treat analysis. The modified intent-to-treat population (the full analysis set) comprised all randomized patients having undergone surgery. The per-protocol population comprised all patients in the full analysis set with valid data for the main endpoint.

With regard to the primary endpoint (Patient Scar Assessment Scale score at 3 months), the 95 percent confidence interval was estimated by a mixed linear model that took account of the stratification criterion. For the secondary criteria, the complication rate was estimated using a generalized linear mixed model. At each visit, 18-month safety and scar quality (according to the Patient Scar Assessment Scale/Observer Scar Assessment Scale scores) were analyzed using a mixed model, to evaluate time-by-effect, group-by-effect, and time-by-group interactions. The aesthetic quality evaluated by the patient and a surgeon was compared using a mixed linear model. The occupational exposure to blood frequencies were described in the two groups. All statistical analyses were performed with SAS software (v9.2; SAS Institute, Inc., Cary, N.C.). For the primary endpoint, the lower 95 percent confidence limit was compared to the noninferiority margin defined at 4 points. For all secondary endpoints, the significance level was defined at 5 percent.

RESULTS

Study Population

From March of 2012 to March of 2013, 664 patients were enrolled and 660 were randomized (Fig. 1). The full analysis set (modified intent-to-treat) and per-protocol populations consisted of 649 and 519 patients, respectively. In the full analysis set at baseline, the two treatment arms did not appear to differ (Table 2). Approximately half of the patients were recruited from plastic surgery departments. Two-thirds of the patients were female, and 55.6 percent were current or former smokers. In the cost-effectiveness analysis, the complete-case population consisted of 434 patients ($n = 214$ in the stapler arm and $n = 220$ in the needle arm) and the population with imputed data consisted of 627 patients (Table 3).

Scar Assessment at 3 Months after Surgery

For the full analysis set ($n = 649$), the mean Patient Scar Assessment Scale score at 3 months

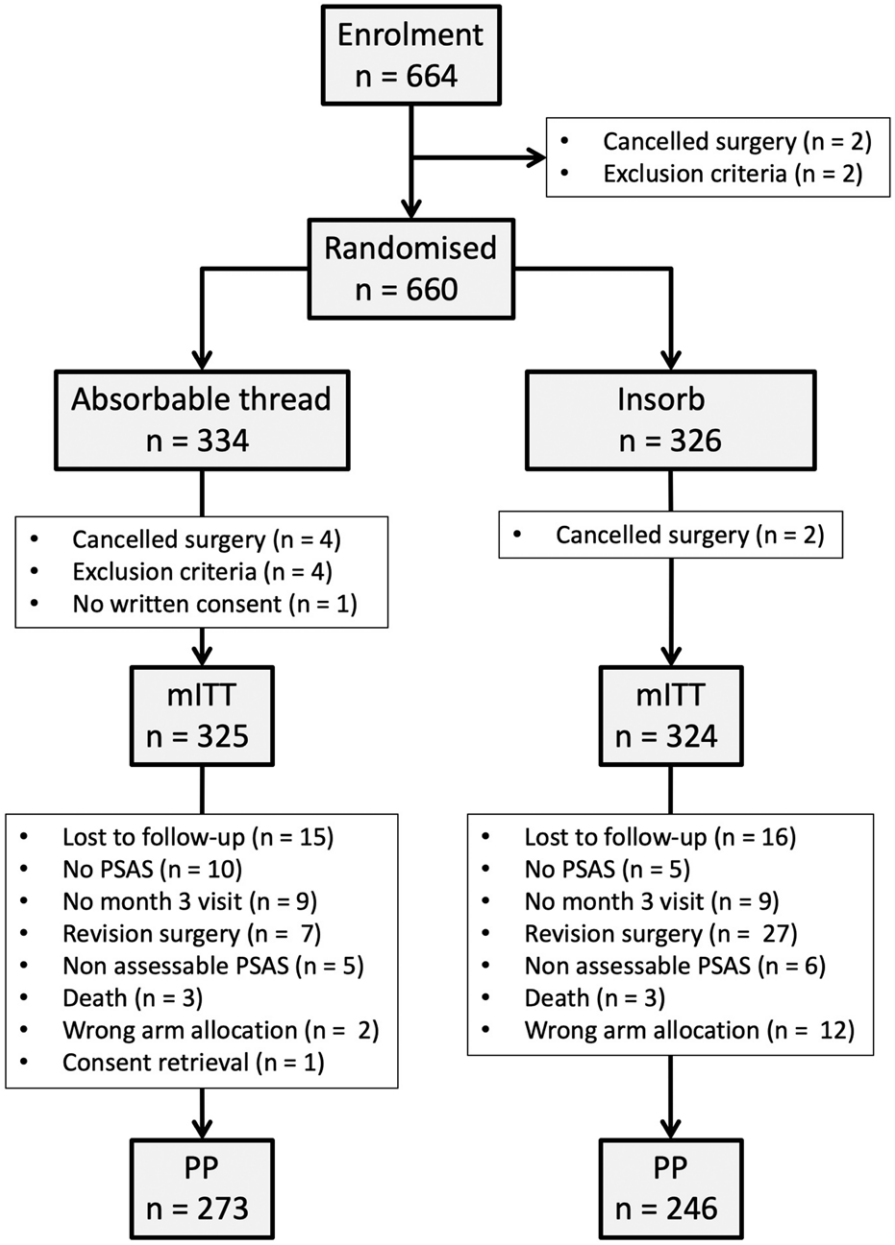


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart. *mITT*, modified intent-to-treat; *PSAS*, Patient Scar Assessment Scale; *PP*, per-protocol.

after surgery was 17.37 (95 percent CI, 13.47 to 21.28) in the stapler arm and 15.68 (95 percent CI, 11.81 to 19.55) in the needle arm (Tables 4 and 5). Thus, the outcome of closure with absorbable suture and a needle had a slightly higher trend than closure with a stapler. However, the mean difference between the two procedures was not significant, and the upper limit of this confidence interval was below the noninferiority level. Thus, with regard to the scar's tolerability (measured by the Patient Scar Assessment Scale score), the stapler was not inferior to absorbable suture. The results were similar in the ear, nose, and throat and plastic surgery departments but differed for the gynecology departments. These findings were similar in the per-protocol population, and they were corroborated by sensitivity analyses.

In both treatment arms, the mean Patient Scar Assessment Scale score fell between 3 and 12 months, then stabilized between 12 and 18 months (Fig. 2). The stapler was found to be noninferior at all time points.

Likewise, the mean Observer Scar Assessment Scale score was lower in the needle arm than in

Table 2. Baseline Characteristics of the Full Analysis Set*

Characteristics	Insorb (%)	Absorbable Suture (%)	Total (%)
No.	324	325	649
Sex			
Male	118 (36.4)	108 (33.2)	226 (34.8)
Female	206 (63.6)	217 (66.8)	423 (65.2)
Age, yr			
Mean ± SD	49.6 ± 13.3	49.0 ± 13.1	49.3 ± 13.2
Median	50	49	49
Range	21–75	18–75	18–75
Type of surgery			
Cervicotomy	130 (40.1)	126 (38.8)	256 (39.4)
Abdominoplasty	163 (50.3)	166 (51.1)	329 (50.7)
Suprapubic surgery	31 (9.6)	33 (10.2)	64 (9.9)
ECOG-PS score			
0	276 (85.2)	278 (85.5)	554 (85.4)
1	48 (14.8)	47 (14.5)	95 (14.6)
Tobacco consumption			
Current smoker	81 (25.0)	100 (30.8)	181 (27.9)
Never-smoker	142 (43.8)	146 (44.9)	288 (44.4)
Former smoker	101 (31.2)	79 (24.3)	180 (27.7)
At least one risk factor for poor wound healing	96 (29.6)	100 (30.8)	196 (30.2)
At least one concomitant treatment	66 (20.4)	67 (20.6)	133 (20.5)

ECOG-PS, Eastern Cooperative Oncology Group performance status.
*Modified intent-to-treat population.

the stapler arm at all time points ($p < 0.0001$) (Fig. 3). The time-by-treatment interaction was not statistically significant ($p = 0.06$), although the difference between the two arms decreased at month 12. Again, the stapler was not inferior to a conventional thread with regard to the scar's tolerability.

Cost-Effectiveness Analysis

As expected, subcuticular closure took longer in the needle arm than in the stapler arm. During the 3-month follow-up period, the patient-reported number of consultations for a suture-related complication was higher in the stapler arm (Table 6).

Although use of the stapler reduced the suturing time, the device was associated with a significantly higher total cost than conventional thread; the additional cost of using the device (estimated using a nonparametric bootstrap resampling method) was €51.57 (95 percent CI, €34.37 to €68.13) for the complete-case population, €52.92 (95 percent CI, €39.99 to €65.97) for the full analysis set, and €116.77 (95 percent CI, €90.22 to €143.61) for the full analysis set with worst values. Regarding the incremental cost-effectiveness ratio, this corresponds to a €146 per additional point of Patient Scar Assessment Scale lost for the complete-case population. However, when considering the full analysis set with imputed values, the use of the stapler dominated; on average, the device was both costlier and less effective than the conventional method.

Table 3. The Two Populations Considered in the Cost-Effectiveness Assessment

Data	No. (%)
Participants with missing data	
Missing data on subcuticular suture material	13 (2.1)
Missing data on suturing time	22 (3.5)
Missing data on 3-mo health care consumption*	154 (24.6)
Missing data on the 3-mo PSAS score	110 (17.5)
At least one item of missing data	193 (30.8)
Populations analyzed	
Complete-case population (no missing data)	434 (69.2)
Population with interpolated data	627 (100)

PSAS, Patient Scar Assessment Scale.
*At least one item of missing data on consumption.

The higher overall cost associated with use of the stapler was mainly attributable to the device's purchase price, which completely offset the reduction in the staff costs associated with the shorter closure time. It should also be noted that the use of the stapler was associated with higher follow-up costs (because of consultations for suture-related complications). These results suggest that the stapler is unlikely to be considered cost-effective; it is significantly costlier than a conventional thread, and does not significantly improve the suturing quality.

To assess the robustness of our results, we performed a sensitivity analysis on the full analysis set, with mean values allocated for missing data. First, as the purchase price of the stapler is likely to fall over time, we estimated the incremental cost-effectiveness ratio for a 50 percent price decrease. Second, we adopted an alternative estimate of the cost of operating room use for a French hospital in 2012.[14] The bootstrapped incremental cost-effectiveness ratios for each of these two scenarios

Table 4. Patient Scar Assessment Scale Score 3 Months after Surgery in the Two Study Arms, According to the Type of Surgical Procedure*

Population Analyzed	No.	Stapler Arm (95% CI)	Needle Arm (95% CI)	Difference (95% CI)
FAS with multiple imputation of missing data	649	17.37 (13.47–21.28)	15.68 (11.81–19.55)	1.69 (0.28–3.10)
Cervicotomy		16.64 (11.58–21.70)	15.83 (10.78–20.88)	0.81 (−0.98 to 2.59)
Abdominoplasty		17.35 (11.67–23.04)	18.19 (12.51–23.88)	−0.84 (−2.35 to 0.67)
Suprapubic surgery		18.13 (9.18–27.08)	13.02 (4.20–21.84)	5.11 (1.40–8.82)
FAS with imputation of the mean score for missing data	649	16.94 (15.21–18.67)	14.81 (13.08–16.54)	2.13 (0.84–3.43)
Cervicotomy		14.91 (12.74–17.09)	14.12 (11.95–16.29)	0.80 (−0.83 to 2.42)
Abdominoplasty		16.76 (14.34–19.18)	17.74 (15.32–20.16)	−0.97 (−2.40 to 0.46)
Suprapubic surgery		19.14 (15.09–23.20)	12.56 (8.52–16.61)	6.58 (3.35–9.81)
Per-protocol population	519	17.03 (14.61–19.45)	14.93 (12.57–17.29)	2.10 (0.54–3.67)
Cervicotomy		14.69 (11.61–17.77)	14.35 (11.36–17.35)	0.34 (−1.65 to 2.33)
Abdominoplasty		17.76 (14.37–21.15)	18.51 (15.14–21.88)	−0.75 (−2.36 to 0.87)
Suprapubic surgery		18.64 (13.01–24.27)	11.92 (6.46–17.39)	6.72 (2.79–10.64)

FAS, full analysis set.
*The data are quoted as the mean (95% CI) score.

significantly reduced the cost of the stapler but not to the extent that it became less costly than a conventional thread (Fig. 4).

Assessment of Other Secondary Objectives

The operating and anesthetic times were similar in the two arms (Table 7). The suturing time was shorter in the stapler arm ($p < 0.0001$), except for suprapubic surgery ($p = 0.0684$). The complication rate 1 week after surgery was similar in the two arms ($p = 0.2933$).

Suturing-related occupational exposure to blood involving surgical staff was less frequent in the stapler arm (0.3 percent) than in the needle arm (2.1 percent). With regard to the scar's aesthetic aspect, the patient-rated and surgeon-rated visual analogue scale scores were in agreement (Fig. 5).

Table 5. Patient Scar Assessment Scale Score 3 Months after Surgery, in the Complete-Case Population

Population	No.	Stapler Arm	Needle Arm
Complete-case population	434		
Mean ± SD		15.59 ± 7.08	15.94 ± 8.36
Median		14.00	14.00
IQR		9.50	10.00
FAS with imputation of the mean subscore value for missing data	627		
Mean ± SD		15.98 ± 6.48	15.44 ± 7.46
Median		15.98	14.00
IQR		6.00	10.00
FAS with multiple imputation of missing data	627		
Mean ± SD		13.98 ± 7.62	14.02 ± 8.19
Median		12.00	12.00
IQR		11.00	11.00

IQR, interquartile range; FAS, full analysis set; PSAS, Patient Scar Assessment Scale.
*Patient Scar Assessment Scale scores are quoted as the mean ± SD, median, and IQR. The lower the score, the more satisfactory the scar outcome.

Safety

Eight patients withdrew from the study before surgery, and five patients were exposed to both the needle technique and the stapler technique. A total of 318 patients were treated with staples, and 339 were exposed to conventional suturing.

Nonserious Adverse Events

A total of 372 nonserious adverse events were reported (Table 8): 206 in 149 patients in the stapler arm, and 166 in 126 patients in the needle arm. Most of these adverse events were local phenomena (e.g., infection, inflammation, and bleeding).

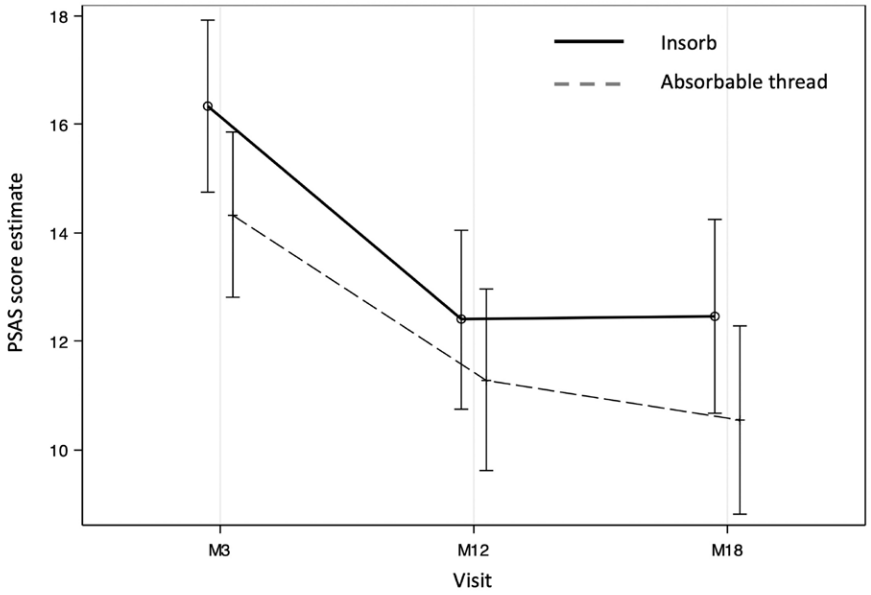
With regard to severity, the great majority of the adverse events were mild [$n = 130$ (63 percent) in the stapler arm; $n = 122$ (73 percent) in the needle arm] or moderate [$n = 66$ (32 percent) in the stapler arm; $n = 40$ (24 percent) in the needle arm]. Local infections were more frequent in the stapler arm, and local inflammation was more frequent in the needle arm (nonsignificant).

Serious Adverse Events and Deaths

No unexpected serious adverse events were observed in either treatment arm. A total of 33 deaths occurred during the study period (15 in the stapler arm and 18 in the needle arm) (Table 9). Most of the documented deaths were linked to progression of the disease that had prompted the surgery.

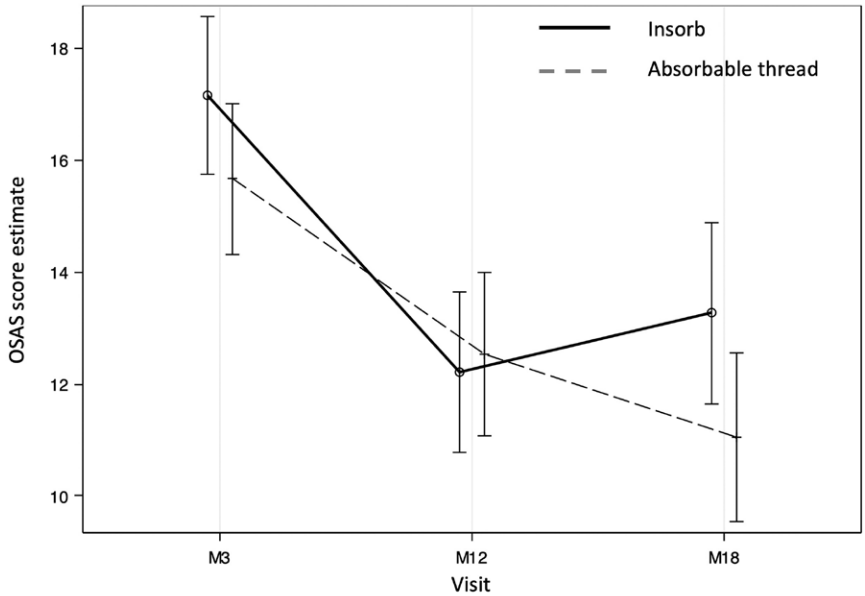
DISCUSSION

Our present results show that the use of a novel stapler for deep dermal suturing was associated with a significantly shorter suturing time and greater safety for surgical staff (lower frequency of occupational exposure to blood). However, the



Visit	Insorb	Absorbable thread	Difference
M3	17.15[15.73;18.56]	15.66[14.32;17.01]	1.49[0.11; 2.86]
M12	12.22[10.78;13.65]	12.54[11.08;13.99]	-0.32[-1.82; 1.18]
M18	13.26[11.64;14.88]	11.04[9.54;12.55]	2.22[0.52; 3.92]

Fig. 2. Change in Patient Scar Assessment Scale score from month 3 to month 18. *PSAS*, Patient Scar Assessment Scale; *M*, month.



Visit	Insorb	Absorbable thread	Difference
M3	16.34 (14.75;17.93)	14.34 (12.80;15.87)	2.00 (0.48; 3.53)
M12	12.41 (10.76;14.05)	11.29 (9.62;12.96)	1.12 (-0.59; 2.83)
M18	12.46 (10.67;14.24)	10.55 (8.81;12.29)	1.91 (0.02; 3.80)

Fig. 3. Change in the Observer Scar Assessment Scale score from month 3 to month 18. *OSAS*, Observer Scar Assessment Scale; *M*, month.

Table 6. Mean Resource Consumption in the Complete-Case Population (*n* = 434)

Resources	Insorb Stapler (%)	Absorbable Thread (%)
No.	214	220
Suture duration, min		
Mean ± SD	6.33 ± 5.07	15.68 ± 8.56
Median	5	15
IQR	4.34	10
Closure		
Sutures per patient, units		
Mean ± SD	0.05 ± 0.53*	3.45 ± 1.88
Median	0*	3
IQR	0	3
Staples per patient		
Mean ± SD	1.55 ± 0.55	—
Median	2	—
IQR	1	—
Follow-up consultations		
0	195 (91.1)	209 (95)
1	8 (3.7)	8 (3.6)
≥1	11 (5.1)	3 (1.4)
OEB	1 (0.5)†	5 (2.3)

IQR, interquartile range; OEB, occupational exposure to blood.
*Two patients randomized into the stapler arm were sutured with absorbable thread because of problems in stapler use.
†As two patients in the stapler arm were sutured with absorbable thread, one case of OEB was recorded in that arm.

operating time was not significantly different: this was because of the overall length of operations reducing the relative part of suturing time. The scar tolerability at 3 months in the stapler arm was not inferior to that observed in the needle arm. This satisfactory outcome for tolerability and aesthetic appearance was maintained at 18 months, as judged by the patient and the surgeon.

The results in the ear, nose, and throat and plastic surgery departments tended to favor the stapler (or did not disadvantage it), whereas the results in gynecology departments tended to favor the needle and thread. There are at least three possible, overlapping explanations: (1) gynecologic incisions are often in the pubic hair region, (2) the incision length is different, and (3) peritoneal opening can modify the postoperative healing process. The stapler's safety profile was not statistically evaluated in this trial.

First, our cost-effectiveness analysis showed that from a societal viewpoint, use of the stapler for deep dermal suturing will not be more expensive than the use of conventional thread, as long as (1) the sales price during the study period (2012 to 2014) is halved, and (2) total operating room costs (rather than solely the personal and consumable costs) are considered. Even though the stapler did not display an advantage with regard to the total cost of suturing in our study, these results require further explanation: one should expect the stapler's main advantage to be the avoidance of the long-term direct and indirect costs associated with occupational exposure to blood (work absence, worker replacement, loss of quality of life, and reduced survival) rather than in-hospital cost savings. However, it is important to note that our estimation of the costs associated with occupational exposure to blood was limited to a 3-month time horizon and was not associated with statistical comparison between arms. Given that occupational exposure to blood is known to generate long-term costs (additional health care resource consumption, loss of quality of life, and reduced survival), the device may be cost-effective if the time horizon is extended to several years. [**See Table, Supplemental Digital Content 1**, which shows a comparison of estimated costs: mean resource consumption in the complete-case population (*n* = 434). This table provide in-depth description of medical consumption regarding medical devices, medical care fees, and occupational exposure to blood, ***http://links.lww.com/PRS/E274***.]

The present study had a number of limitations. First, the proportion of missing data (30.8 percent) in the cost-effectiveness analysis was relatively high: although 660 patients were randomized, the complete-case population consisted of only 434 patients. However, as shown in Table 3, the proportion of missing data never exceeded 25 percent per type of item. Second, and as mentioned above, the time horizon for the cost-effectiveness analysis (3 months) was relatively short.

Even if the results are in line with previous data, the present study also had a number of strengths. Previous studies were limited to a small number of patients and none of them were statistically managed. First, this multicenter study was performed across a broad network of university hospitals throughout France and in three different surgical contexts (ear, nose, and throat; plastic surgery; and gynecology). Despite potential intercenter differences in practice (minimized by adherence to the study protocol), the results can probably be extrapolated to all such establishments of this type in France and perhaps to similar establishments in other countries. Second, our implementation of a prospective study design avoided the potential selection, misclassification, and/or information biases associated with retrospective designs. Third, this was the first study to investigate the potential safety gains, time savings, and cost savings associated with a novel subcuticular stapler in Europe (rather than in the United States).

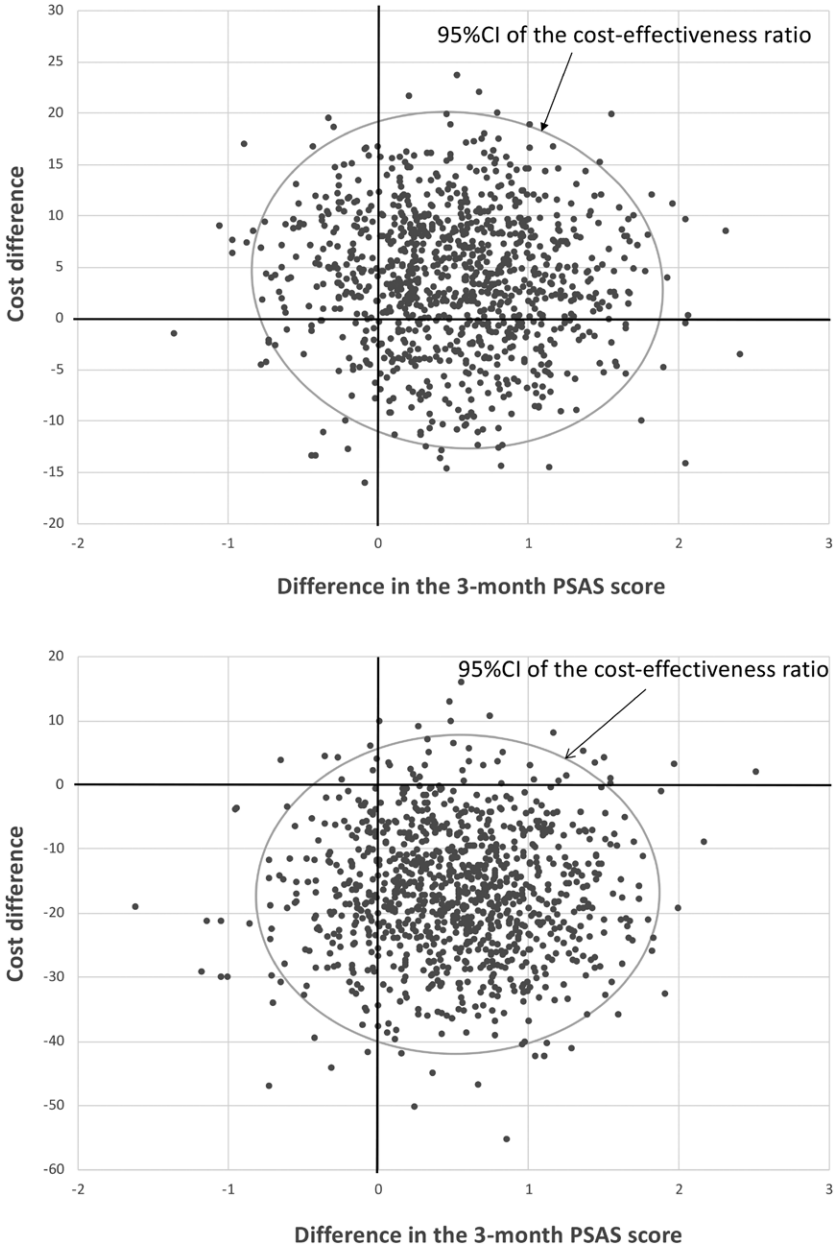
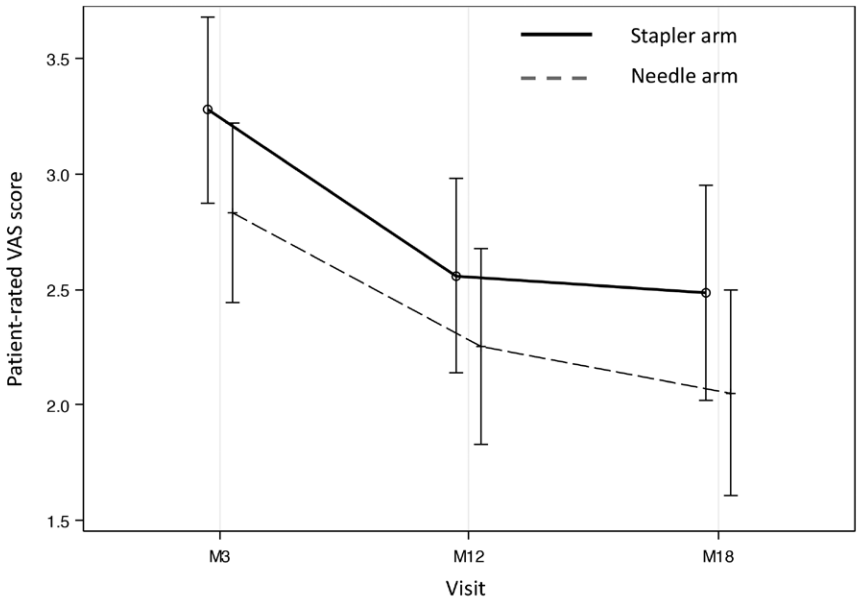


Fig. 4. Bootstrap plots and confidence interval on the cost-effectiveness plane for a 50 percent decrease in the cost of the stapler (*above*), and bootstrap plots and confidence interval on the cost-effectiveness plane for alternative estimation of the operating room expenses per minute (*below*). *PSAS*, Patient Scar Assessment Scale.

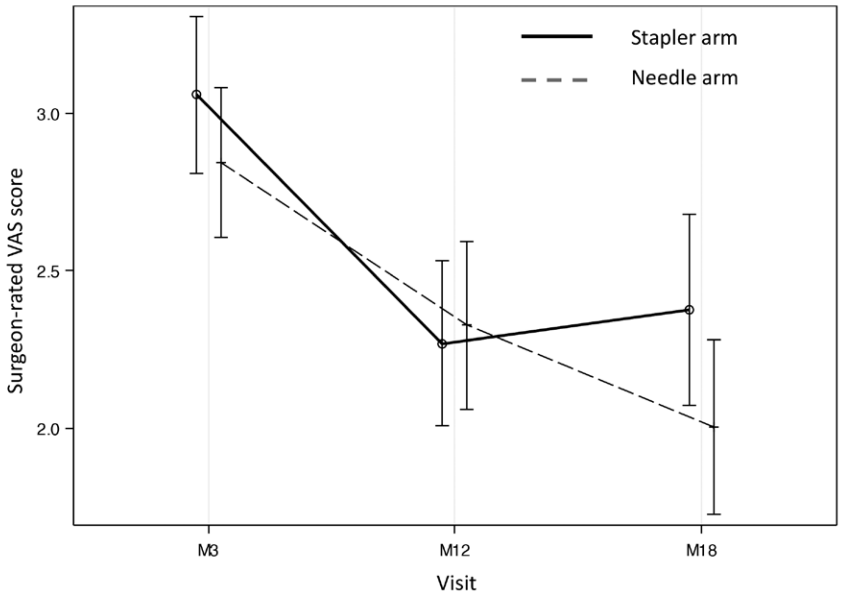
Table 7. Anesthesia, Operating, and Suturing Times as a Function of the Type of Surgery and the Type of Closure*

Time	Stapler Arm (95% CI)	Suture Arm (95% CI)	Difference (95% CI)	*p*
Anesthesia time	3:54 (3:15–4:33]	3:55 (3:17–4:34)	–0:01 (–0:19 to 0:17)	0.8975
Operating time	3:00 (2:29–3:31)	2:59 (2:28–3:30)	0:01 (–0:15 to 0:17)	0.8967
Suturing time	0:07 (0:05–0:09)	0:14 (0:12–0:16)	–0:06 (–0:08 to –0:05)	<0.0001
Cervicotomy	0:07 (0:05–0:10)	0:13 (0:11–0:16)	–0:06 (–0:07 to –0:04)	<0.0001
Abdominoplasty	0:08 (0:05–0:11)	0:20 (0:17–0:22)	–0:11 (–0:12 to –0:10)	<0.0001
Suprapubic	0:05 (0:01–0:10)	0:08 (0:04–0:13)	–0:03 (–0:06 to 0:00)	0.0684

*Data are expressed as the mean (95 percent CI) duration in hours:minutes.



Visit	Stapler arm	Needle arm	Difference
M3	3.28 (2.88;3.68)	2.83 (2.44;3.22)	0.45 (0.04;0.86)
M12	2.56 (2.14;2.98	2.26 (1.83;2.68)	0.30 (-0.16;0.77)
M18	2.49 (2.02;2.95	2.05 (1.61;2.50)	0.43 (-0.08;0.95)



Visit	Stapler arm	Needle arm	Difference
M3	3.06 (2.81;3.31)	2.84 (2.60;3.08)	0.22 (-0.05;0.48)
M12	2.27 (2.01;2.53)	2.33 (2.06;2.59)	-0.06 (-0.36;0.25)
M18	2.38 (2.07;2.68)	2.00 (1.73;2.28)	0.37 (0.03;0.72)

Fig. 5. Aesthetic scar quality as rated by the patient (*above*) and the surgeon (*below*) on a visual analogue scale. *VAS*, visual analogue scale; *M*, month.

Table 8. Summary of Nonserious Adverse Events in Each Treatment Arm, by System-Organ Class

	Stapler Arm				Needle Arm			
System Organ Class	No. of AEs*	No. of Patients*	% of Patients in the Arm*	% of Patients Exposed	No. of AEs*	No. of Patients*	% of Patients in the Arm*	% of Patients Exposed
Cardiac disorders	1	1	0.3	0.3	0	0	0	0
Gastrointestinal disorders	4	4	1.2	1.3	3	2	0.60	0.6
General disorders and administration site conditions	62 (63)	60 (61)	18.4 (18.7)	18.8	79 (78)	73 (72)	21.86 (21.5)	21.5
Infections and infestations	16	16	4.9	5.0	14	13	3.89	3.8
Injury, poisoning, and procedural complications	51 (52)	44 (45)	13.5 (13.8)	13.8	40 (39)	36 (35)	10.78 (10.5)	10.6
Neoplasms, benign, malignant, and unspecified	1	1	0.3	0.3	1	1	0.30	0.3
Nervous system disorders	0	0	0	0	2	2	0.60	0.6
Product issues	57	55	16.9	17.2	20	20	5.99	5.9
Reproductive system and breast disorders	1	1	0.3	0.3	1	1	0.30	0.3
Respiratory, thoracic, and mediastinal disorders	1	1	0.3	0.3	0	0	0	0
Skin and subcutaneous tissue disorders	2	2	0.6	0.6	2	2	0.60	0.6
Surgical and medical procedures	4	4	1.2	1.3	1	1	0.30	0.3
Vascular disorders	4	4	1	1.3	5	5	1.50	1.5
Total	204 (206)	147 (149)	45.1 (45.7)	45.9	168 (166)	128 (126)	38.32 (37.7)	37.8
Total no. of patients randomized in the arm		326					334	

AEs, adverse events.
*Values in parentheses indicate treatment exposure deviations taken into account.

Table 9. Details of Deaths during the Study Period

	Stapler Arm	Needle Arm	Total
No. of deaths caused by disease progression	10	11*	21
No. of deaths resulting from other causes	5 – Hemorrhagic shock/inhalation (D6) – Hemorrhagic shock (carotid artery rupture/stroke (M1) – Not documented (M2, ≥M2, M3)	7 – Pulmonary embolism (D3) – Carotid artery rupture (M1) – Not documented (M2, M4, M6 × 2, M12)	12
Total no.	15	18	33

D, day; M, month.
*In the needle arm, two of the deaths subsequently linked to disease progression were initially notified as serious adverse events.

CONCLUSIONS

Use of a semiautomatic stapler for deep dermal suturing in gynecologic; ear, nose, and throat; and plastic surgery in French university hospitals provided wound healing outcomes that were not worse than with conventional suturing. The use of this new device is associated with a noninferiority for outcomes and time, a minimally higher cost. Higher safety should be further confirmed in larger studies.

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The trial is registered under the name "Medico-economic Evaluation of Subcutaneous Automatic Resorbable Staples Device (S2CARA)," ClinicalTrials.gov identification no. NCT01546272 (https://clinicaltrials.gov/ct2/show/NCT01546272).

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