ECONOMIC ANALYSIS OF ENZYMATIC DEBRIDEMENT VERSUS STANDARD BURN CARE: A RETROSPECTIVE ANALYSIS

ANALYSE MÉDICO-ÉCONOMIQUE COMPARATIVE RÉTROSPECTIVE DE L'EXCISION ENZYMATIQUE ET DU TRAITEMENT STANDARD DES BRÛLÉS

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SUMMARY. When compared to standard surgical management, rapid enzymatic debridement of deep burns reduces the need for surgery while achieving similar long-term results. However, few studies have directly compared the costs of standard surgical and enzymatic burn care. We conducted a study comparing the care costs of 44 adult burn patients treated before (n=22) and after (n=22) introducing rapid bromelain-based enzymatic debridement (BED) of deep burns. Mean age was 59 years, 54% were male, and mean total body surface area (TBSA) was 23.5%. Burn etiology included flame and scalding burns (8). Groups treated with standard of care and enzymatic debridement were comparable in terms of age, sex and TBSA. Burn management with BED significantly reduced total debridement costs as well as grand total costs when compared with traditional surgical care. Such reduction was mostly related to lower costs associated with reduced surgical care and less facilities and resources consumption in the BED group.

Keywords: bromelain-based enzymatic debridement, NexoBrid®, cost, enzymatic burn care

RÉSUMÉ. *Comparativement au traitement standard, l'excision enzymatique précoce (EEP) réduit la nécessité de chirurgie, à résultats égaux à long termes. Très peu d'études ont comparé les coûts de ces deux stratégies. Nous avons comparé 2 groupes de 22 patients profondément brûlés ayant pour l'un été pris en charge conventionnellement, l'autre ayant bénéficié d'une EEP. L'âge moyen était de 59 ans, 54% étaient des hommes, la surface brûlée moyenne de 23,5% (les 2 groupes étaient comparables). Seuls 8 patients avaient été ébouillantés, les autres étant brûlés par flamme. L'utilisation d'EEP réduisait significativement le coût de la prise en charge, en rapport avec la réduction de l'utilisation de locaux et de matériel consécutifs à la chirurgie.*

Mots-clés : *excision enzymatique, Nexobrid®, brûlure, coûts*

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Introduction

Burns are among the most severe of all injuries. The depth of injury is especially important since many of the local and systemic complications (i.e., inflammation, infection, sepsis) as well as the healing potential are related to it. Early removal of the eschar is essential to limit the local and systemic complications as well as to allow visualization of the underlying wound bed to determine its viability.[1-4] Traditionally, eschar removal has been accomplished by tangential excision, in which sequential removal of the eschar is performed in the operating room via dermatomes until viable tissue is reached. This surgical removal requires specialized personnel and facilities and contributes to further trauma to the patient (from blood loss and anesthesia). Additionally, due to its non-selective nature, surgical excision often results in the removal of viable dermal elements that may have been beneficial for conservative secondary healing.[5] In most cases of surgical debridement, the remaining wound bed is covered with a skin autograft, resulting in further patient morbidity. More recently, enzymatic debridement with a bromelain-based agent (BED) has been shown to be as effective as surgical treatment, yet more selective, resulting in a reduced need for surgical excision, as well as fewer and smaller skin graft donor sites, with comparable long-term outcomes.[6,7] Since its approval in Europe in 2017, early enzymatic debridement has become part of the standard of care (SOC) for deep partial and full thickness burns, and specific guidelines and recommendations have been published at European and national level.[8,9]

With increases in medical costs and shrinking healthcare budgets worldwide, there is a greater need than ever to find therapies that optimize patient outcomes while being as cost effective as possible. Because enzymatic debridement is a minimally invasive modality that allows early burn debridement and reduces the need for surgery and prolonged hospitalization, we hypothesized that it would be less costly than standard, surgically-based burn care. Previous observations based on DRGs and cost simulation, but not actual costs, were published in the literature.[10,11] The objective of the current study was to compare the actual costs of surgical and enzymatic debridement and the following reconstruction phase in a group of burn patients treated at a large burn center in Italy.

Materials and methods

We conducted a retrospective chart review of patients treated in the burn unit of a large academic hospital in Italy before and after introducing rapid enzymatic debridement. The study was approved by the Institutional Review Board (Number 2214CESC) with waiver of informed consent due to the retrospective nature of the study.

We included adult patients with deep partial or full thickness burns in need of debridement. The first group of patients were the last 22 patients treated with standard surgical excision followed by autografting prior to February 2017, when enzymatic debridement was introduced into the practice of our center. The second group of patients included the first 22 patients treated with rapid enzymatic debridement after February 2017 (excluding the first 10 that we considered as a learning phase). Patients with chemical or electrical burns were excluded as well as pregnant patients or those with burns already saturated with silver sulfadiazine. We also excluded patients with chronic steroid use or known sensitivity to pineapple or bromelain from the second, enzymatic debridement group.

Structured chart review was performed by trained physicians blinded to patient identity and not involved directly in the patients' clinical care. Basic demographic and clinical data were collected, including burn etiology, location, % total body surface area (TBSA) burned, and depth of burn. We also collected detailed information regarding all patient procedures (nature, site, timing, duration, personnel, blood product transfusion, materials and facilities). For the purposes of calculating costs of enzymatic debridement, we calculated the cost of the product (NexoBrid® - Mediwound Germany GmbH, Eisenstraße 5, 65428 Rüsselsheim am Main, Germany) by multiplying the %TBSA by 2 gr. We also collected data regarding care after hospital discharge, e.g., time to wound closure and scar outcomes.

The primary study outcome was total debridement costs associated with patient care. The secondary outcome was grand total costs of burn patient management. The actual specific expenses at our hospital were used to calculate the hospitalization-, resources- and surgery-related costs.

Patient data were summarized using descriptive statistical methods. The analysis was carried out using Stata MP17 software. Continuous variables were expressed as mean ± standard deviation and range or as median, interquartile range (IQR) and range; categorical variables were expressed as proportions. The normality and homoscedasticity of the continuous variables were evaluated; for those not normally distributed, a normalization model has been built, where possible. Normal or normalized continuous variables were compared between groups using the student t test for independent data; non-normalized data were compared by the Wilcoxon rank sum test; categorical variables were compared between groups by chi-square test or Fisher's exact test. A p-value <0.05 was considered significant for all tests.

Results

The study included 44 patients, 22 in each of the two study groups. A comparison of baseline patient and burn characteristics is presented in *Table I*. No significant differences occurred in the baseline characteristics between the two groups. Main outcomes are summarized in *Table II*. Result details are presented in *Supplementary Tables I-IX*.

Table I - Baseline characteristics of the study groups

	SOC	NexoBrid®	p-value
Mean (range) age, years	54,9 (29-84)	53,5 (21-92)	0.799
Males n. (%)	16 (72.7)	17 (77.3)	0.728
Etiology n (%) Flame Scalds	 15 (68.2) 7 (31.8)	 14 (63.6) 8 (36.4)	0.750
Mean (range) %TBSA	23.0 (11-38)	23.8 (5-46)	0.821
Mean (range) %TBSA treated	20.5 (5-38)	19.6 (2-46)	0.773
Comorbidities, n. (%)	10 (45.5)	9 (40.9)	0.761

SOC: standard of care; TBSA: total body surface area

Table II - Summary of outcomes

Cost Factor	SOC, median (range), €	NexoBrid®, median (range), €	P value
Hospital days before debridement	6.720 (3.840-12.260)	1.130 (0-6.500)	<.0001
Preop checkup	99,6 (99,6-199,2)	0 (0-99,6)	<.0001
Human resources for Debridement	977,9 (204,0-3.129,5)	194,4 (100,2-400,8)	<.0001
Device costs including NXB	1.464,2 (409,3-2.354,7)	5.997,2 (758,8-15.300,0)	<.0001
Transfusion	649,4 (0,0-2.018,0)	108,5 (0,0-1.318,0)	<.0001
Operating room fee	75,1 (15,3-160,1)	65,8 (0,0-300,0)	0.67
Total debridement (primary outcome)	12.042,0 (6.989,7-23.507,2)	9.752,4 (2.988,1-24.523,5)	0.016
Human resources for reconstruction	355,4 (0,0-2.092,3)	614,9 (0,0-2.848,7)	0.044
Hospitalization total costs	48,498.0; (20,648.0-84,480.0)	25,784.0; (11,316.0-72,000.0)	<0.001
Fix fee costs	13,023.2; (5,477.9-22,436.1)	9,132.6; (3,938.8-20,365.3)	0.005
Grand total costs (secondary outcome)	65,116.0; (27,389.7-112,180.6)	45,663.1; (19,694.0-101,826.7)	0.005

SOC: standard of care; TBSA: total body surface area; NXB: NexoBrid®

The mean number of hospital days prior to debridement was 6,6 for SICU and 0,4 for ICU, with a mean pre-debridement cost of €6720. The 22 patients required 26 surgical debridement procedures (mean 1.2/patient). Surgeon time varied from procedure to procedure (mean 110.7/procedure). The median surgeon costs for session was €468,6. Mean anesthesiologist time was 214,8 minutes per procedure with a median cost of €222. Median cost for the scrub nurse who worked for a mean of 137,5 minutes per procedure was €173,9. In addition, nurse anesthetists worked for a mean of 214,8 minutes per procedure at a median cost of €87. The total median cost of human resources per procedure was €977,9.

Each of the procedures required a mean of €75,1 for setting up the operating room and €107,6 in disposable anesthetic equipment. Mean dressing cost was €1369,6 per procedure. Thus, the total median cost of materials was €1464,2 per procedure. The SOC patients received a mean of 2,5 units of blood at a mean cost of €467,5 per procedure and a mean of 2,1 units of plasma products at a mean cost of €181,9 per procedure. Thus, the total mean cost of blood and plasma per procedure was €649,4.

When all personnel, facility and equipment costs are added up, the median total cost for debridement was €12.042. Hospitalization total costs amounted to €48,498.

The median grand total costs in the group of patients treated with standard care, including debridement, reconstruction, hospitalization expenses and fixed costs, was €65.116.

The mean number of hospital days prior to debridement was 0,7 for SICU and 0,6 for ICU, with a mean pre-debridement cost of €1130. The 22 patients required 28 enzymatic debridement procedures (mean 1.27/patient). Surgeon time varied from procedure to procedure (mean 60.2/procedure). The median surgeon costs per session was €72. Mean anesthesiologist time was 53.2 minutes per procedure with a median cost of €36. Median cost for the scrub nurse who worked for a mean of 61.7 minutes per procedure was €28,2. In addition, nurse anesthetists worked for a mean of 54.5 minutes per procedure at a median cost of €14,1. The total median cost of human resources per procedure was €194,4.

Each of the procedures required a mean of €65,8 for setting up the operating room and €50,5 in disposable anesthetic and conscious sedation equipment. Mean dressing cost was €65,8 per procedure. Median BED cost per procedure was €5873. Thus, the total median cost of materials was €5.997,2 per procedure. The BED patients received a mean of 0,1 units of blood at a mean cost of €25,5 per procedure and a mean of 1 unit of plasma products at a mean cost of €83 per procedure. Thus, the total mean cost of blood and plasma per procedure was €108,5.

When all personnel, facility and equipment costs are added up, the median total cost for debridement was €9752,4. Hospitalization total costs amounted to €25,784.

The median grand total costs in the group of patients treated with BED, including debridement, reconstruction, hospitalization expenses and fixed costs, was €45.663,1.

Discussion

In this observational study, we compared the total costs of care of 22 burn patients managed with standard surgical care compared with 22 burn patients treated with early enzymatic debridement using NexoBrid®. In terms of costs, we found that management with BED significantly reduced total debridement, total debridement plus reconstruction, and total hospitalization as well as grand total costs when compared with traditional surgical care (*Fig. 1,2: Table II*). Such reduction was mostly related to lower costs associated with less surgical care and facilities and resources consumption in the enzymatic debridement group. Please note that pure reconstructive surgery costs were actually higher in our observation in the BED group (supplementary *Table VII*). This is counter-intuitive to our daily practice, in which many patients heal spontaneously with minimal reconstructive surgery after enzymatic debridement; this finding might be related to the circumstance that even excluding the absolute first 10 patients, the 22 pa-

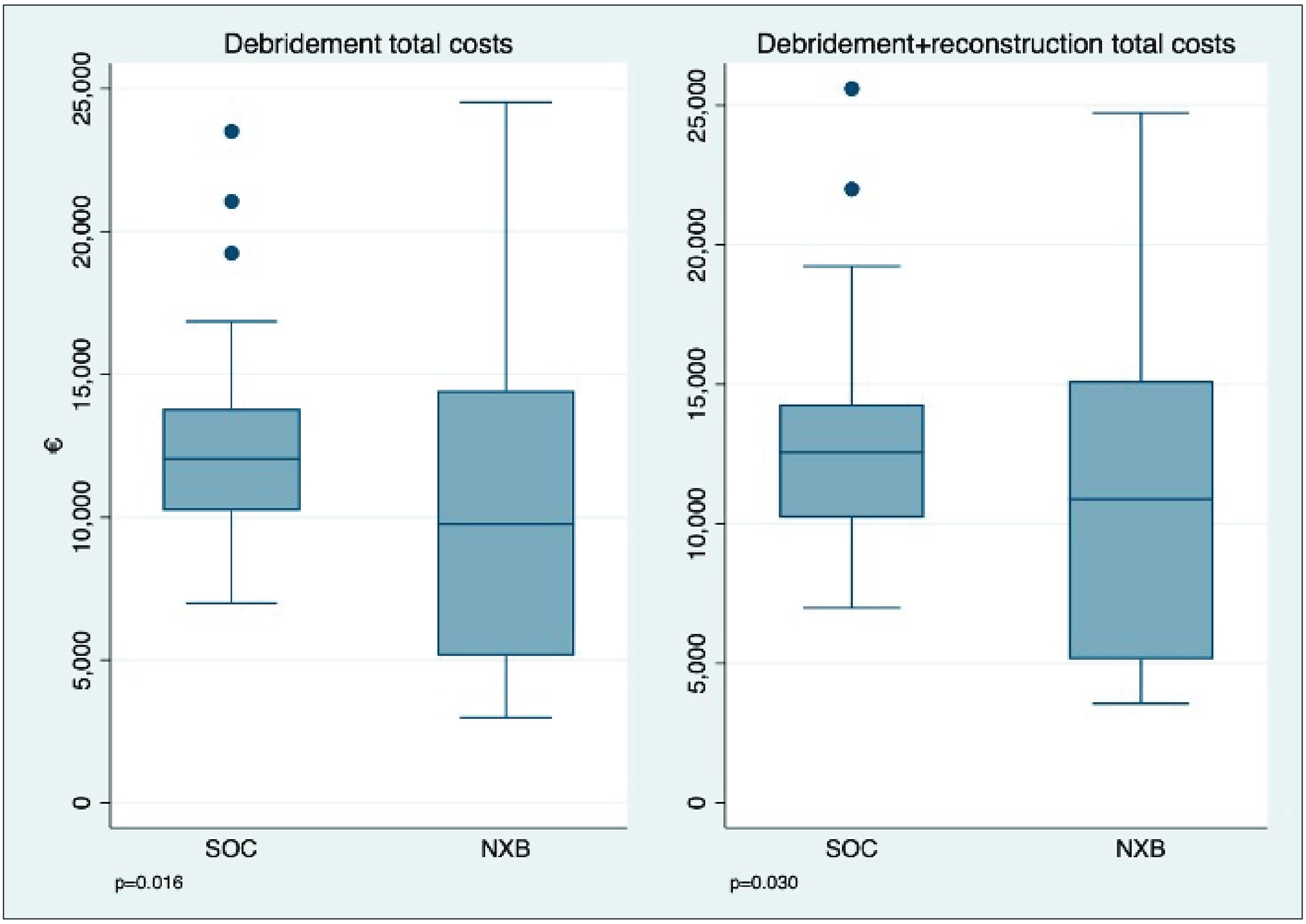

Fig. 1 - Comparison of total debridement and debridement + reconstruction costs; the median value of the NexoBrid® group is significantly lower than the standard of care group in both cases (p=0.0016 and p=0.030 respectively).

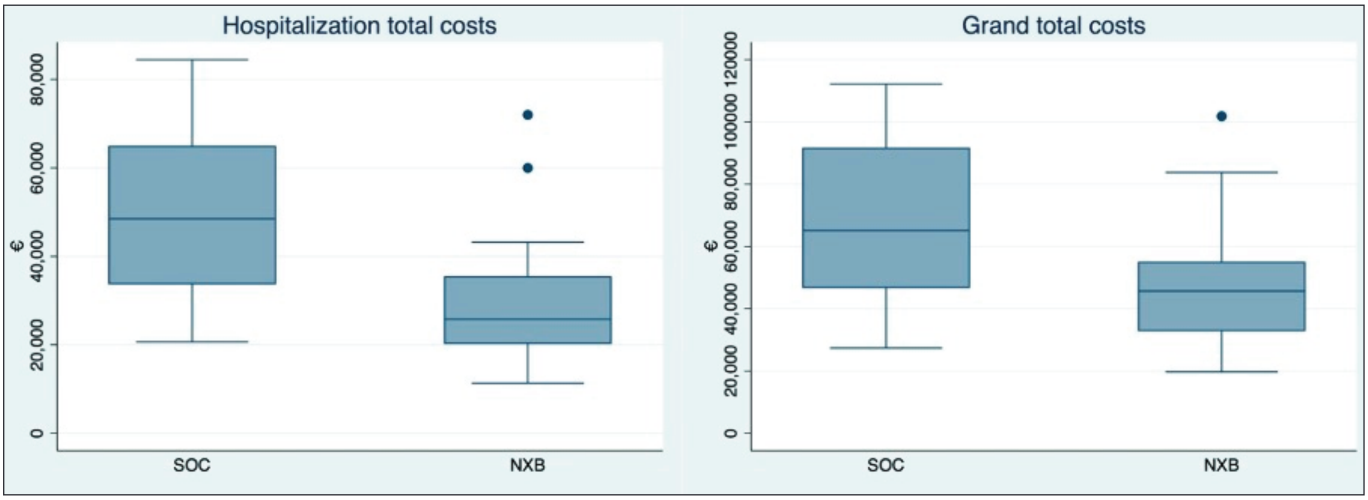

Fig. 2 - Comparison of total hospitalization and grand total costs; the median value of the NexoBrid® group is significantly lower than the standard of care group in both cases (p<0,001 and p<0,005 respectively).

tients included in the study were still early in our experience with BED; therefore we might have over-treated with reconstructive surgery areas that, as we later learned, could possibly heal on their own with conservative dressings. We believe that with a more numerous population sample, this finding would likely equalize between the 2 groups or shift in favour of the BED group. Nevertheless, even accounting for this unexpected finding and study cohort limitation, debridement plus reconstruction costs were still significantly lower in the BED patient group. Hospitalization costs were also significantly lower in the BED patients group, both in the SICU and ICU setting, directly related to a lower hospitalization period in the BED group.

The reduced cost of early enzymatic debridement adds up to its widely reported benefits when compared to surgical tangential excision, including the decreased number and size of skin graft donor sites, reduced blood loss and patient morbidity, and improved long-term cosmetic and functional outcomes.[6,7]

Care of burn patients is complex, requiring a large number of highly trained professionals and extensive resources. The population of burn victims is very heterogeneous in terms of underlying conditions, severity and co-morbidities. Thus, calculating total costs associated with their care is not a simple task. Even more so, there are wide variations at the local, regional and national levels with regards to costs and methods of reimbursement. The constant struggle to deliver complex and costly care in an era of shrinking resources is quite challenging. Burn centers need to be prepared for unexpected surges in demand, for example in the event of burn mass-casualty incidents. These incidents may occur anywhere and at any time as a result of acts of terror, natural disasters or industrial accidents. Generally, burn victims in such instances are taken to the nearest burn center that often lacks the personnel, skills and resources to deal with the surge in care requests. Thus, methods to deliver high quality, non-surgical and more cost-effective burn care are greatly needed. This has been exemplified successfully in the recent Bucharest night club fire disaster, where 39 burn victims were treated with early enzymatic debridement by local personnel trained by two international burn experts over the course of 2 days.[12] Therefore, the use of early enzymatic debridement agent that preserves uninjured viable dermis offers a minimally invasive modality, which is an alternative to traditional surgical burn care. This minimal invasive approach reduces dependency on scarce and limited highly-specialized surgical facilities and healthcare professionals.

As per our results, one can appreciate that SOC is more expensive than enzymatic debridement-based care, reducing the mean total debridement cost from €12.042 to €9.752,4 (p=0,016) and the mean total debridement plus reconstruction cost from €12.557,1 to €10.883,6 (p=0,030). Both SOC and BED methods require a similar number of procedures, however enzymatic debridement is generally achieved much earlier (*Supplementary Table I*) than surgical debridement, resulting in significant cost saving by reducing hospital length of stay. Enzymatic debridement also reduces costs associated with operating room facilities and personnel, effectively increasing the available surgical facilities without further *investments*, and freeing specialized professionals for other highly demanded and highly reimbursable surgical procedures. With regards to materials costs, the cost of BED and associated dressings is significantly greater than the dressing costs used for SOC, mostly due to the cost of BED itself. However, this cost difference is compensated by the reduction in hospital and facility costs noted above with enzymatic debridement. Additional cost savings also come from a significant reduction in the need for blood and blood products, such as fresh frozen plasma when compared with the SOC.

We feel a final important note is necessary. In many centers in Italy, burn specific DRGs are meant to cover the forbidding expenses of burn care, allowing hospitals to maintain this service. Unfortunately, DRGs do not cover all of the expenses or the needed investment in modern burn care and, as a result, many hospitals suffer from a continuous struggle for resources, thus many hospitals refrain from having burn units at all. Reduced cost of care may offset this negative balance, allowing DRGs to effectively cover burn care expenses.

Our study has several notable limitations. The current study was a before and after study and not a randomized controlled trial. Therefore, it is subject to residual confounding known and unknown variables. We also could not check for any other systematic changes that may have occurred at our center over the course of the study that may have affected study outcomes. Our study is limited to a single center and may not be representative of other burn centers where costs and practices may differ. For instance, at our center, BED is always applied in the OR. However as per guidelines,[8,9] it can be applied at patient bedside with proper analgesia, and many centers in Italy effectively do this, further reducing the associated costs and facilities use.[8-11] Early enzymatic debridement is a novel approach that has a learning curve. Thus, our results may differ over time with even greater experience. Finally, our study sample was relatively small and might have been underpowered to detect subtler differences in some of the outcomes.

Conclusions

In a semi-consecutive case series of 44 patients with deep partial or full thickness burns, half of which were managed with standard burn care and the other half with early enzymatic debridement, the use of BED was less expensive, mostly due to reduced surgery and hospitalization resources related costs. Such a benefit of early enzymatic debridement in terms of cost savings is highly promising but needs to be confirmed by larger cohort studies.

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Supplementary Table I - Pre-treatment hospitalization, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
Days in subintensive therapy; mean±SD (range)	6.6±1.4 (4-9)	0.7±1.1 (0-4)	3.7±3.3 (0-9)	<0.0001
Days in intensive care; mean±SD (range)	0.4±1.2 (0-5)	0.6±1.2 (0-5)	0.5±1.2 (0-5)	0.195
Pre-treatment costs (€); median; range IQR (range)	6,720; 4,800-7,680 (3,840-12,260)	1,130; 0-2,600 (0-6,500)	4,320; 1,130-6,720 (0-12,260)	<0.0001

Supplementary Table II - Procedural characteristics of debridement, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
n. of treatments; n (%)				0.721
• 1	18 (81.8)	16 (72.7)	34 (77.3)	
• 2	4 (18.2)	6 (27.3)	10 (22.7)	
Ward: n (%)				<0.0001
• ICU	0 (0.0)	9 (40.9)	9 (20.5)	
• OR	0 (0.0)	7 (31.8)	7 (15.9)	
• OR + ICU	0 (0.0)	1 (4.6)	1 (2.3)	
• OT	22 (100.0)	0 (0.0)	22 (50.0)	
• SICU	0 (0.0)	5 (22.7)	5 (11.3)	
Pre-operational check-up costs (€); median; range IQR (range)	99.6 99.6-99.6 (99.6-199.2)	0.0 0.0-99.6 (0-99.6)	99.6 0.0-99.6 (0.0-199.2)	<0.0001

Supplementary Table III - Characteristics of human resources needed for debridement, by treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
t. of surgical treatment I (min); mean±SD (range)	110.7±59.7 (21-240)	60.2±6.1 (50-75)	85.5±49.1 (21-240)	0.001
t. of surgical treatment II (min); mean±SD (range)	137.5±95.9 (30-251)	61.7±5.2 (55-70)	92.0±67.9 (30-251)	0.195
n. of surgical treatment I; n (%)	3.3±1.1 (2-6)	1.2±0.4 (1-2)	2.2±1.3 (1-6)	<0.0001
n. of surgical treatment II; n (%)	3.8±0.5 (3-4)	0.7±0.5 (0-1)	1.9±1.7 (0-4)	0.007
Surgeon costs (€); median; range IQR (range)	468.6; 252.0-698.4 (50.4-1,699.2)	72.0; 72.0-144.0 (60.0-168.0)	147.0; 72.0-486.6 (50.4-1,699.2)	0.023
t. of nurse treatment I (min); mean±SD (range)	137.5±95.9 (30-251)	61.7±5.2 (55-70)	115.6±96.7 (55-305)	<0.0001
t. of nurse treatment II (min); mean±SD (range)	137.5±95.9 (30-251)	61.7±5.2 (55-70)	120.6±106.8 (30-251)	0.435
n. of nurse treatment I; n (%)	2	0.8±0.4 (0-1)	1.4±0.7 (0-2)	-
n. of nurse treatment II; n (%)	2	1	1.4±0.5 (1-2)	-
Nurse costs (€); median; range IQR (range)	173.9; 113.7-286.7 (53.6-515.1)	28.2; 28.2-56.4 (0.0-56.4)	56.4; 28.2-173.9 (0.0-515.1)	<0.0001
t. anesthetist (min); mean±SD (range)	214.8±132.8 (57-548)	53.2±53.9 (0-120)	134.0±129.3 (0-548)	<0.0001
Anesthetist costs (€); median; range IQR (range)	222.0; 145.2-363.6 (68.4-657.6)	36.0; 0.0-144.0 (0.0-144.0)	144.0; 36.0-222.0 (0.0-657.6)	<0.0001
t. nurse anesthetist (min); mean±SD (range)	214.8±132.8 (57-548)	54.5±52.9 (0-120)	134.6±128.7 (0-548)	<0.0001
Nurse Anesthetist costs (€); median; range IQR (range)	87.0; 56.9-142.4 (26.8-257.6)	14.1; 0.0-56.4 (0.0-56.4)	56.4; 14.1-87.0 (0.0-257.6)	<0.0001
Total cost of human resources (€); median; range IQR (range)	977.9; 546.7-1,543.0 (204.0-3,129.5)	194.4; 128.4-312.6 (100.2-400.8)	344.4; 186.1-977.9 (100.2-3,129.5)	<0.0001

Supplementary Table IV - Characteristics of device consumption needed, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
n. of procedures; n (%) • 1 • 2	19 (86.4) 3 (13.6)	18 (81.8) 4 (18.2)	37 (84.1) 7 (15.9)	1.000
Dressing devices costs (€); median; range IQR (range)	1,369.6; 1,205.3-1,850.7 (314.7-2,165.3)	65.8; 41.8-68.1 (31.6-131.6)	223.1; 65.8-1,369.6 (31.6-2,165.3)	<0.0001
NXB costs (€); median; range IQR (range)	-	5.873; 2,517-10,068 (672-15,102)	5.873; 2,517-10,068 (672-15,102)	-
Anesthesia kit costs (€); mean±SD (range)	107.6±33.2 (94.7-189.3)	34.4±46.6 (0.0-94.7)	71.0±54.4 (0.0-189.3)	<0.0001
Analgo-sedative kit costs. (€); mean±SD (range)	0	15.9±28.4 (0.0-100.0)	8.0±21.4 (0.0-100.0)	0.009
Devices total costs (€); media; range IQR (range)	1,464.2; 1,300.0-1,945.3 (409.3-2,354.7)	5,997.2; 2,582.7-10,136.1 (758.8-15,300.0)	1,945.3; 1,454.8-5,997.2 (409.3-15,300.0)	<0.0001

Supplementary Table V - Characteristics of transfusions needed, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
n. of blood units; mean±SD (range)	2.5±2.3 (0-8)	0.1±0.5 (0-2)	1.3±2.0 (0-8)	<0.0001
Blood units. costs (€); mean±SD (range)	467.5±434.7 (0.0-1,496.0)	25.5±87.4 (0.0-374.0)	246.5±382.1 (0.0-1,496.0)	<0.0001
n. of plasma units; mean±SD (range)	2.1±2.2 (0-9)	1.0±3.2 (0-13)	1.5±2.8 (0-13)	0.004
Plasma units costs (€); mean±SD (range)	181.9±191.6 (0.0-783.0)	83.0±277.0 (0.0-1,131.0)	132.5±240.6 (0.0-1,131.0)	0.004
Total transfusion costs (€); mean±SD (range)	649.4±590.0 (0.0-2,018.0)	108.5±316.4 (0.0-1,318.0)	379.0±542.0 (0.0-2,018.0)	<0.0001

Supplementary Table VI - Characteristics of the total costs of debridement, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
O.R. FEE (€); mean±SD (range)	75.1±38.2 (15.3-160.1)	65.8±04.7 (0.0-300.0)	70.4±71.6 (0.0-300.0)	0.672
Total costs (€); median; range IQR (range)	9,633.6; 8,179.1-11,034.5 (5,591.8-18,805.8)	7,801.9; 4,119.2-11,536.3 (2,390.5-19,618.8)	9,455.0; 6,218.9-11,040.7 (2,390.5-19,618.8)	0.016
Fix fee costs (€); median; range IQR (range)	2,408.4; 2,044.8-2,758.6 (1,397.9-4,701.4)	1,950.5; 1,029.8-2,884.1 (597.6-4,904.7)	2,363.7; 1,554.7-2,760.2 (597.6-4,904.7)	0.016
Grand total costs (€); median; range IQR (range)	12,042.0; 10,223.8-13,793.1 (6,989.7-23,507.2)	9,752.4; 5,149.1-14,420.3 (2,988.1-24,523.5)	11,818.7; 7,773.6-13,800.9 (2,988.1-24,523.5)	0.016

Supplementary Table VII - Characteristics of the human resources needed for reconstructive surgery, per treatment

Variable	SOC (n=22)	NXB (n=22)	Totale (n=44)	p-value
n. of procedures; n (%) • 0 • 1 • 2 • 3	 12 (54.6) 9 (40.9) 0 (0.0) 1 (4.5)	 4 (18.2) 12 (54.6) 5 (22.6) 1 (4.6)	 16 (36.4) 21 (47.6) 5 (11.4) 2 (4.6)	0.013
t. of procedure I (min); mean±SD (range)	86.0±26.6 (32-134)	69.0±38.2 (20-159)	75.1±35.0 (20-159)	0.224
t. of procedure II (min); mean±SD (range)	113	46.2±34.8 (16-107)	55.7±40.6 (16-113)	-
t. of procedure III (min); mean±SD (range)	63	86	74.5±16.3 (63-86)	-
n. of surgeons procedure I; n (%)	2.7±0.7 (2-4)	3.0±1.0 (2-5)	2.9±0.9 (2-5)	0.395
n. of surgeons procedure II; n (%)	2	2.3±1.5 (1-5)	2.3±1.4 (1-5)	1.000
n. of surgeons procedure III; n (%)	3	4	3.5±0.7 (3-4)	-
Surgeon costs (€); mean±SD (range)	151.1±225.4 (0.0-876.0)	275.7±333.5 (0.0-1,522.8)	213.4±288.3 (0.0-1,522.8)	0.051
t. of nurse procedure I (min); mean±SD (range)	140.1±40.9 (53-190)	115.6±53.0 (56-249)	124.3±49.7 (53-249)	<0.0001
t. of nurse procedure II (min); mean±SD (range)	137.5±95.9 (30-251)	61.7±5.2 (55-70)	120.6±106.8 (30-251)	0.217
n. of nurse treatment I; n (%)	185	107.0±54.7 (58-210)	118.1±58.0 (58-210)	-
n. of nurse treatment II; n (%)	136	149	142.5±9.2 (136-149)	-
n. of nurse; n (%)	1.0±1.0 (0-2)	2.6±0.8 (0-2)	1.3±1.0 (0-2)	0.013
Nurse costs (€); mean±SD (range)	73.6±107.1 (0.0-438.0)	122.7±117.3 (0.0-477.5)	98.1±113.7 (0.0-477.5)	0.045
t. anesthetist (min); mean±SD (range)	172.2±111.0 (56-508)	158.3±116.5 (56-508)	163.3±112.7 (53.508)	0.559
Anesthetist costs (€); mean±SD (range)	93.9±136.7 (0.0-559.2)	155.5±146.5 (0.0-609.6)	124.7±143.5 (0.0-609.6)	0.044
t. of nurse anesthetist (min); mean±SD (range)	172.2±111.0 (53-466)	158.3±116.5 (56-508)	163.3±112.7 (53-508)	0.657
Nurse anesthetist costs (€); mean±SD (range)	36.8±53.6 (0.0-219.0)	60.9±57.4 (0.0-238.8)	48.8±56.2 (0.0-238.8)	0.044
Human resources total costs (€); median; range IQR (range)	355.4±518.9 (0.0-2,092.3)	614.9±640.2 (0.0-2,848.7)	485.0±590.6 (0.0-2,848.7)	0.044

Supplementary Table VIII - Characteristics of total hospitalization, per treatment

Variable	SOC (n=22)	NXB (n=22)	Total (n=44)	p-value
Days of hospitalization; mean±SD (range)	48.5±21.3 (22-88)	34.0±14.1 (13-75)	41.3±19.3 (13-88)	0.009
Days of SICU; mean±SD (range)	46.7±21.2 (19-88)	29.8±14.3 (9-75)	38.2±19.8 (9-88)	0.002
SICU costs (€); median; range IQR (range)	38,400; 28,800-64,320 (18,240-84,480)	25,440; 20,160-25,440 (8,640-72,000)	29,760; 24,000-43,200 (8,640-84,480)	0.002
Days of ward; mean±SD (range)	1.1±2.5 (0-9)	0.5±1.1 (0-4)	0.8±1.9 (0-9)	0.424
Ward costs (€); mean±SD (range)	390.9±844.6 (0-3,096)	156.4±278.7 (0-1,376)	273.6±657.6 (0-3,096)	0.424
Days of ICU; mean±SD (range)	4.0±5.1 (0-14)	0.7±1.9 (0-7)	2.3±4.1 (0-14)	0.020
ICU costs (€); mean±SD (range)	4,963.6±6,563.3 (0.0-18,200.0)	945.5±2,413.2 (0.0-9,100.0)	2,954.5±5,292.6 (0.0-18,200.0)	0.027
Hospitalization total costs (€); median; range IQR (range)	48,498.0; 33,660.0-65,008.0 (20,648.0-84,480.0)	25,784.0; 20,160.0-35,520.0 (11,316.0-72,000.0)	34.930.0; 24,030.0-51,792.0 (11,316.0-84,480.0)	<0.001

Supplementary Table IX - Characteristics of total debridement + reconstruction, total cost, fixed costs and grand total costs, per treatment

Variable	**SOC (n=22)**	**NXB (n=22)**	**Total (n=44)**	**p-value**
Total treatment costs + reconstructive surgery (€); median; range IQR (range)	12,557.1; 10,223.8-14,275.9 (6,989.7-25,559.5)	10,883.6; 5,149.1-15,122.6 (3,551.1-24,725.5)	12,168.8; 8,006.4-14,494.8 (3,551.1-25,599.5)	0.030
Total costs (€); median; range IQR (range)	52,092.8; 37,287.8-73,405.5 (21,911.8-89,744.5)	36,530.5; 26,199.2-44,100.8 (15,755.2-81,461.4)	42,092.3; 28,797.8-55,095.2 (15,755.2-89,744.5)	0.005
Fix fee costs (€); median; range IQR (range)	13,023.2; 9,321.9-18,351.4 (5,477.9-22,436.1)	9,132.6; 6,549.8-11,025.2 (3,938.8-20,365.3)	10,523.1; 7,199.5-13,773.8 (3,938.8-22,436.1)	0.005
Grand total costs (€); median; range IQR (range)	65,116.0; 46,609.7-91,756.8 (27,389.7-112,180.6)	45,663.1; 32,749.1-55,126.0 (19,694.0-101,826.7)	52,615.4; 35,997.3-68,869.0 (19,694.0-112,180.6)	0.005