

Open Abdomen with Negative-Pressure Wound Therapy versus Primary Fascial Closure in Abdominal Septic Shock: A Propensity-Weighted Cohort Study

Nicolò Sella

University of Padova

Alberto Friziero

Padova University Hospital

Tommaso Pettenuzzo

tommaso.pettenuzzo@unipd.it

University of Padova

Giorgia Togniolo

University of Padova

Martina Della Libera

University of Padova

Alessandro Parolin

University of Padova

Eugenio Garofalo

Magna Graecia University

Mara Bassi

University of Padova

Andrea Bruni

University of Calabria, Arcavacata di Rende

Piero Dissegna

University of Padova

Alessandro De Cassai

University of Padova

Elisa Pistollato

University of Padova

Nicola Baldan

Padova University Hospital

Marco Brolese

Padova University Hospital

Paolo Navalesi

University of Padova

Michele Valmasoni

Padova University Hospital

Annalisa Boscolo

University of Padova

Research Article

Keywords: abdominal septic shock, open abdomen, ABThera, negative-pressure wound therapy, propensity-score overlap weighting

Posted Date: September 24th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10956494/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background.

To evaluate whether initial open-abdomen management with negative-pressure wound therapy (OA-NPWT) was associated with 30-day mortality compared with primary fascial closure in patients undergoing urgent surgery for abdominal septic shock, while accounting for confounding by indication.

Methods.

We conducted a retrospective single-center cohort study of consecutive adults undergoing urgent source-control laparotomy between May 2021 and April 2026. Propensity-score overlap weighting was used to balance pre-decision clinical and operative characteristics. The primary outcome was 30-day mortality. Exploratory analyses assessed factors associated with OA-NPWT selection and treatment-effect heterogeneity.

Results.

Among 128 patients, 52 (40.6%) received OA-NPWT and 76 (59.4%) underwent primary fascial closure. After overlap weighting, estimated 30-day mortality was 24.8% with OA-NPWT and 23.9% with primary closure (risk difference, 0.9 percentage points; 95% CI, -18.4 to 20.2; RR, 1.04; 95% CI, 0.47–2.29). Sensitivity and time-to-event analyses were concordant. OA-NPWT was associated with longer mechanical ventilation. Its selection was associated mainly with shorter operative duration, second-vasoconstrictor use, and procedure type. No reproducible clinical or baseline-risk subgroup showed a differential mortality effect.

Conclusions.

Initial OA-NPWT management was not associated with a detectable difference in 30-day mortality after adjustment for confounding by indication, although clinically important benefit or harm could not be excluded. These findings support selective rather than routine open-abdomen use in abdominal septic shock.

Clinical trial registration

Not applicable. This was a retrospective observational cohort study.

Background

Severe intra-abdominal sepsis complicated by septic shock remains a major challenge in emergency surgery. Although timely source control is essential, the optimal abdominal management after laparotomy is uncertain. In selected patients, primary fascial closure may be undesirable because of profound physiological derangement, bowel edema, concern for intra-abdominal hypertension, the need for deferred anastomosis or planned re-exploration, or uncertainty regarding source control. Accordingly, international guidelines recognize the open abdomen (OA) as a potential damage-control strategy in carefully selected patients [1, 2].

Negative-pressure wound therapy (NPWT) is widely used for temporary abdominal closure. The ABThera™ system has been specifically described for OA-NPWT management in septic patients and may facilitate evacuation of contaminated fluid, reduce visceral edema, limit fascial retraction, and allow rapid re-entry for staged procedures [2, 3]. Recent clinical reports have illustrated its use in septic shock following intestinal perforation, permitting delayed reconstruction after physiological stabilization [4]. Experimental data also suggest that negative peritoneal pressure may reduce the burden of inflammatory mediators, although this biological effect remains unproven in humans [5, 6].

Observational studies have reported improved survival with OA and NPWT compared with primary closure or alternative temporary closure methods [7, 8], while standardized OA protocols have achieved favorable survival and high delayed fascial closure rates in selected patients [9, 10]. However, these findings are difficult to interpret because OA is preferentially used in patients with greater physiological instability and more complex intra-abdominal disease, creating substantial confounding by indication. Moreover, OA carries important potential harms, including repeated operations, fluid and protein losses, prolonged ventilation, enteroatmospheric fistula, and failure of definitive fascial closure [1, 2]. Comparative evidence remains inconsistent, and randomized evidence is still limited [5, 11].

Given this uncertainty, the primary aim of this study was to evaluate the association between an initial OA-NPWT strategy using and 30-day mortality compared with primary fascial closure, using propensity-score overlap weighting. Two exploratory aims were to identify preoperative and intraoperative factors associated with OA-NPWT use and to investigate whether its association with mortality varied according to selected clinical characteristics or baseline predicted risk.

Methods

Study design and setting

We conducted a retrospective, single-center observational cohort study at a university tertiary-care hospital serving as a regional referral center for emergency and complex abdominal surgery. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (AOP60652). The requirement for written informed consent was managed according to local regulations. Reporting followed the STROBE statement (**Supplementary Table 1**).

Study population

We included consecutive adults (≥ 18 years) with abdominal septic shock undergoing urgent surgery for source control between May 1, 2021, and April 30, 2026. Septic shock was defined according to the Sepsis-3/Surviving Sepsis Campaign criteria [12]. We excluded patients with abdominal sepsis without septic shock, patients undergoing abdominal source control for trauma, and patients in whom an open abdomen was instituted after an initial elective operation.

Objectives and outcomes

The primary objective was to estimate the association between an initial open-abdomen negative-pressure wound therapy (OA-NPWT) strategy and 30-day mortality compared with primary fascial closure, accounting for confounding by indication. Secondary outcomes included duration of mechanical ventilation, tracheostomy, 28-day ventilator-free days (VFDs), continuous renal replacement therapy, abdominal reinterventions, abdominal wound dehiscence, multidrug-resistant organism (MDRO) infection, and ICU and hospital length of stay. Exploratory analyses investigated factors associated with OA-NPWT use and potential heterogeneity of its association with mortality.

Exposure and data collection

Exposure was defined according to the strategy selected at the index source-control laparotomy: OA-NPWT or primary fascial closure, irrespective of subsequent reoperations or delayed closure. OA-NPWT was performed using the ABThera™ Open Abdomen Negative Pressure Therapy System at -100 mmHg.

Demographic, clinical, laboratory, physiological, and operative variables were retrospectively extracted from electronic medical records, anesthesia charts, operative reports, and ICU records using a predefined database. Variables included comorbidities, preoperative severity and inflammatory markers, Mannheim Peritonitis Index, timing and type of surgery, intraoperative hemodynamic support, blood loss and transfusions, and postoperative outcomes. Detailed variable definitions, including VFDs, abdominal reintervention, wound dehiscence, MDRO infection, second vasoconstrictor use, and OA-NPWT duration, are provided in the Supplementary Methods.

Statistical analysis

Continuous variables were summarized as mean (SD) or median (IQR), and categorical variables as counts and percentages. For the primary analysis, the propensity score for OA-NPWT use was estimated using logistic regression including prespecified variables available before or at the time of the decision for open-abdomen management. Overlap weighting was used to target patients with the greatest clinical

equipoise [15]. Covariate balance was assessed using standardized mean differences, with $|SMD| < 0.10$ considered adequate.

The adjusted 30-day mortality risk ratio (RR) was estimated using overlap-weighted modified Poisson regression with robust variance [16]. Adjusted risks and risk differences were obtained by marginal standardization with 95% confidence intervals. Complementary time-to-event analyses included weighted Kaplan–Meier estimates, restricted mean survival time, and weighted Cox regression. Secondary outcomes were analyzed using weighted regression models appropriate to outcome type.

Missing covariates included in the primary propensity-score model were handled using multiple imputation by chained equations (10 datasets) [19]; outcomes were not imputed. Prespecified sensitivity analyses evaluated the robustness of the primary findings using alternative confounding-control strategies, common-support restriction, complete-case analysis, inclusion of procalcitonin, and E-values [18].

Exploratory analyses of predictors of OA-NPWT use, treatment-effect modification, and baseline mortality risk used penalized regression and bootstrap resampling.

All tests were two-sided, with $P < 0.05$ considered statistically significant for the primary analysis. Analyses were performed using R version 4.5.2.

Additional methodological details are provided in the **Supplementary Methods**.

Results

Study population and covariate balance

During the study period, 179 patients were assessed for eligibility. After excluding 10 patients with abdominal sepsis without septic shock, 38 undergoing abdominal source control for trauma, and 3 in whom an open abdomen was instituted after an initial elective operation, 128 patients comprised the final cohort (**Figure 1**). Of these, 52 (40.6%) received initial open-abdomen management with OA-NPWT and 76 (59.4%) underwent primary fascial closure. Thirty-one deaths occurred within 30 days. Day-30 vital status was known for 120 patients; 8 patients last known alive before day 30 were excluded from the binary mortality analysis but retained in time-to-event analyses with censoring.

The causal framework used to select covariates for adjustment is shown in **Supplementary Figure 1**. Relevant baseline imbalances were present before weighting (**Table 1; Figure 2**), whereas overlap weighting achieved adequate balance across propensity-score covariates. The effective sample size was 37.4 for OA-NPWT and 44.1 for primary closure. No OA-NPWT patient underwent an upper-gastrointestinal procedure, resulting in negligible contribution of this stratum to the overlap estimand.

Association between initial OA-NPWT and clinical outcomes

In the primary overlap-weighted analysis, 30-day mortality was 24.8% with OA-NPWT and 23.9% with primary fascial closure, corresponding to a risk difference of 0.9 percentage points (95% CI, -18.4 to 20.2) and an adjusted RR of 1.04 (95% CI, 0.47-2.29) (**Table 2**).

The time-to-event analyses were concordant. Overlap-weighted cumulative 30-day mortality was 23.9% with OA-NPWT and 22.8% with primary fascial closure. Restricted mean survival time through day 30 was 25.09 versus 25.42 days, corresponding to a difference of -0.33 days (95% bootstrap CI, -4.44 to 3.61). The weighted Cox analysis yielded an HR of 1.05 (95% bootstrap CI, 0.38–2.62), with no evidence of proportional-hazards violation (weighted Schoenfeld-residual test, $P=0.379$). Among the 52 patients initially managed with OA-NPWT, recorded device-placement duration was a median of 47.3 hours (IQR, 38.0–95.3 hours; range, 18–250 hours), equivalent to 1.97 days (IQR, 1.58–3.97 days). The recorded OA-NPWT treatment period had ended by day 2 in 28 of 52 patients (53.8%) and by day 5 in 47 of 52 (90.4%) (**Figure 3**).

Among secondary outcomes, OA-NPWT was associated with more abdominal reinterventions and longer mechanical ventilation, whereas wound dehiscence was less frequent; estimates for the remaining secondary outcomes were imprecise (**Table 2**).

Prespecified sensitivity analyses yielded results consistent with the primary estimate, including conventional multivariable adjustment, propensity-score matching, common-support restriction, complete-case analysis, and reintroduction of procalcitonin (**Supplementary Figure 2**). The E-value for the primary adjusted RR was 1.24; because its 95% CI crossed the null, the E-value for the confidence-limit closest to the null was 1.00.

Factors associated with initial OA-NPWT selection

In the exploratory ridge-penalized model, OA-NPWT use was associated mainly with shorter operative duration, use of a second vasoconstrictor, surgical procedure type, and, more weakly, higher intraoperative norepinephrine requirements (**Figure 4**; **Supplementary Table 2**). Other severity, inflammatory, transfusion, and physiological variables showed weaker associations.

Exploratory treatment-effect heterogeneity

No prespecified modifier showed convincing evidence of treatment-effect heterogeneity (**Table 3**; **Supplementary Figure 3**). Similarly, treatment effects across quartiles of predicted baseline mortality risk were imprecise and showed no consistent trend (**Table 3**; **Supplementary Figure 4**); the continuous treatment-by-risk interaction was not significant. Overall, no reproducible clinical characteristic or

baseline-risk subgroup was identified in which OA-NPWT was associated with a clearly different 30-day mortality effect.

Missing data are fully reported in **Supplementary Table 3**.

Discussion

In this cohort of patients undergoing urgent laparotomy for abdominal septic shock, initial open-abdomen management with OA-NPWT was associated with no detectable difference in 30-day mortality compared with primary fascial closure after adjustment for confounding by indication. Secondary analyses suggested a more intensive postoperative course with open-abdomen management, including more subsequent abdominal procedures and longer mechanical ventilation and critical-care exposure. Exploratory analyses indicated that OA-NPWT was preferentially selected in specific operative settings and in patients with greater hemodynamic instability, whereas no reproducible subgroup was identified in which it was associated with superior survival.

The principal finding was the absence of a detectable mortality advantage with an initial open-abdomen strategy. However, the wide confidence intervals remained compatible with clinically important benefit or harm and therefore preclude any conclusion of equivalence. Our findings do not support routinely leaving the abdomen open with the expectation of improving survival, but neither do they exclude a clinically relevant benefit or harm in appropriately selected patients.

This finding differs from several observational studies reporting lower mortality with open-abdomen negative-pressure therapy. Bleszynski et al. found lower adjusted mortality with open abdomen and VAC than with primary closure in severe abdominal sepsis [7], while Poillucci et al. reported lower 30-day mortality with NPWT compared with alternative temporary closure techniques [8]. A meta-analysis of observational studies similarly suggested lower mortality among patients managed with NPWT [20]. These studies, however, differed substantially in comparators, indications, case mix, and methods used to address baseline severity. Most importantly, the decision to leave the abdomen open is closely linked to physiological instability, operative findings, and anticipated need for staged source control, making observational comparisons particularly vulnerable to confounding by indication. Our use of overlap weighting specifically targeted patients in whom either initial strategy was clinically plausible and may partly explain the difference from previous unweighted or conventionally adjusted comparisons.

Available randomized evidence does not resolve this uncertainty. The Intraperitoneal Vacuum Trial reported improved 90-day survival with OA-NPWT compared with Barker's vacuum pack, but included only 45 patients and compared two temporary abdominal closure techniques rather than open abdomen with primary fascial closure [21]. Likewise, prospective evidence favoring OA-NPWT over Barker's technique addresses device selection after the decision to leave the abdomen open has already been made [22]. Conversely, a recent comparison of open and closed abdominal management found no statistically significant survival difference [11]. Thus, contemporary NPWT appears effective for managing an abdomen that has already been left open, but available evidence does not establish that

choosing an open-abdomen strategy improves survival over primary closure. This distinction is central to the ongoing COOL trial (NCT03163095), which directly compares open versus closed abdominal management after source-control laparotomy for severe intra-abdominal sepsis [5].

The secondary outcomes help characterize the treatment burden associated with open-abdomen management. After weighting, OA-NPWT was associated with approximately 2.8 additional days of mechanical ventilation, 3.3 fewer ventilator-free days, 1.5 additional subsequent abdominal procedures, 3.5 additional ICU days, and 6.9 additional hospital days. These findings should not be interpreted uniformly as adverse effects of OA-NPWT. Planned re-exploration, staged source control, bowel reassessment, and delayed fascial closure are intrinsic components of many open-abdomen pathways, while prolonged ventilation and critical-care exposure may similarly reflect the broader treatment trajectory rather than direct device-related harm. Previous studies have reported favorable fascial-closure and complication profiles with contemporary NPWT systems compared with older temporary closure techniques [22, 23], whereas enhanced NPWT strategies have shown potential advantages in wound clearance or procedural burden without consistent effects on length of stay or mortality [24–26]. The lower incidence of wound dehiscence observed with OA-NPWT should also be interpreted cautiously because the outcome is not symmetrical between strategies. Moreover, this was one of several secondary outcomes assessed without adjustment for multiplicity and should therefore be considered hypothesis-generating.

Exploratory analyses were consistent with selective use of OA-NPWT as part of a damage-control strategy. OA-NPWT use was most strongly associated with a second vasoconstrictor, shorter operative duration, and procedure type, with a weaker association with higher norepinephrine requirement. This pattern is consistent with previous descriptions of open-abdomen management in patients with hemodynamic instability, visceral edema, uncertain bowel viability, deferred reconstruction, or anticipated re-exploration [10, 26, 27], and with reports of staged management in intestinal perforation and septic shock requiring substantial vasopressor support [4]. The association with shorter operative duration may therefore reflect abbreviated laparotomy rather than an effect of the device itself. These characteristics should not be regarded as validated indications for OA-NPWT; rather, they illustrate the clinical selection process underlying treatment allocation and the resulting potential for confounding by indication.

No convincing treatment-effect heterogeneity was identified across SOFA score, Mannheim Peritonitis Index, C-reactive protein, norepinephrine requirement, operative duration, maximum intraoperative lactate, or baseline predicted mortality risk. Although favorable outcomes have been reported in selected patients undergoing abbreviated laparotomy, deferred anastomosis, or planned second-look procedures [3, 4, 21, 28], such reports identify settings in which OA-NPWT can be used successfully rather than demonstrating that these characteristics modify its effect relative to primary closure. Our findings therefore do not support defining thresholds of physiological severity above which OA-NPWT should preferentially be used. However, with only 128 patients and 31 deaths, interaction analyses were

necessarily imprecise, and absence of statistically detectable heterogeneity should not be interpreted as evidence that treatment effects are uniform across all patients.

From a clinical perspective, these findings support a selective rather than routine open-abdomen strategy. The decision to leave the abdomen open should remain driven by operative and physiological circumstances—such as adequacy of source control, bowel viability, anticipated fascial-closure tension, or need for planned re-exploration—rather than by an expectation of a generalized survival benefit. The additional procedural and critical-care burden associated with the open-abdomen pathway should also be considered when weighing its potential technical advantages.

For future research, the key question is therefore not simply whether OA-NPWT is effective once an abdomen has been left open, but which patients benefit from choosing an open-abdomen strategy over primary closure. Beyond the ongoing COOL trial [5], future multicenter studies should ideally enroll patients at the point of genuine surgical equipoise, after initial source control but before the final decision regarding fascial closure, and prospectively capture the intraoperative and technical factors that influence that decision. Randomized or pragmatic designs should standardize the main open-abdomen and closure pathways, account for major operative phenotype and physiological severity, and consider patient-centered outcomes incorporating mortality, organ-support burden, major surgical morbidity, and successful definitive fascial closure rather than mortality alone.

Several limitations warrant consideration. The retrospective, single-center design leaves the possibility of residual confounding despite a prespecified causal framework, restriction of the propensity-score model to pre-decision variables, overlap weighting, and concordant sensitivity analyses. Although overlap weighting achieved excellent balance in measured pre-decision characteristics, treatment allocation may also have depended on unmeasured intraoperative or technical factors not captured in the propensity-score model, including bowel viability, perceived adequacy of source control, visceral or abdominal-wall edema, anticipated fascial-closure tension, need for planned re-exploration, or other elements of surgeon judgment. Residual confounding by indication therefore remains possible despite the observed covariate balance. The limited number of events resulted in wide confidence intervals for the primary effect and particularly low precision for interaction analyses; penalized modeling, spline methods, and bootstrap procedures reduce overfitting but cannot overcome limited information. Positivity was imperfect for some operative categories, especially upper-gastrointestinal surgery; accordingly, the overlap-weighted estimand applies primarily to patients for whom either strategy was realistically possible. Missing covariates were addressed using multiple imputation, while eight patients without complete 30-day follow-up were excluded from the binary outcome but retained with censoring in time-to-event analyses, which yielded concordant findings. Finally, secondary duration-based outcomes are influenced by survival and by the treatment pathway itself, and both exploratory aims should be regarded as hypothesis-generating.

Conclusions

In patients undergoing urgent laparotomy for abdominal septic shock, OA-NPWT was used selectively as a damage-control strategy in the setting of greater physiological instability and specific operative scenarios. After adjustment for measured confounding by indication, no detectable difference in 30-day mortality emerged compared with primary fascial closure, although clinically important benefit or harm could not be excluded. Open-abdomen management was associated with a more intensive postoperative pathway, including more reinterventions and greater exposure to mechanical ventilation and prolonged hospitalization. No reliable clinical or baseline-risk subgroup with a survival advantage was identified. These findings support selective rather than routine use of OA-NPWT, guided by specific operative and physiological indications for avoiding immediate fascial closure rather than by an expectation of improved survival. Larger prospective randomized studies are needed to define its comparative effectiveness more precisely.

Abbreviations

CI, confidence interval; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; MDRO, multidrug-resistant organism; NPWT, negative-pressure wound therapy; OA, open abdomen; OA-NPWT, open-abdomen negative-pressure wound therapy; RR, risk ratio; SD, standard deviation; SMD, standardized mean difference; SOFA, Sequential Organ Failure Assessment; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; VAC, vacuum-assisted closure; VFDs, ventilator-free days.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Padova University Hospital ethics committee under approval number AOP60652, 26/08/2026.

The requirement for individual written informed consent was obtained according to the requirements of the national regulation.

Consent for publication

Not applicable.

Availability of data and materials

Deidentified participant-level data and the analytic code supporting the findings of this study may be made available by the corresponding author upon reasonable request, subject to approval by the

participating institutions and ethics committees and in accordance with applicable data-protection regulations.

Competing interests

The authors declare that they have no conflicts of interest related to this work.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. No equipment, drugs, or other material support was provided for this study.

Authors' contributions

Nicolò Sella: Conceptualization, Methodology, Investigation, Project administration, Writing – original draft, Writing – review & editing. Alberto Friziero: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft, Writing – review & editing. Tommaso Pettenuzzo: Methodology, Formal analysis, Validation, Writing – review & editing. Giorgia Togniolo: Investigation, Data curation, Validation, Writing – review & editing. Martina Della Libera: Investigation, Data curation, Resources, Writing – review & editing. Alessandro Parolin: Investigation, Data curation, Validation, Writing – review & editing. Eugenio Garofalo: Methodology, Validation, Writing – review & editing. Mara Bassi: Investigation, Data curation, Validation, Writing – review & editing. Andrea Bruni: Methodology, Validation, Writing – review & editing. Piero Dissegna: Investigation, Data curation, Validation, Writing – review & editing. Alessandro De Cassai: Methodology, Formal analysis, Validation, Writing – review & editing. Elisa Pistollato: Investigation, Data curation, Resources, Writing – review & editing. Nicola Baldan: Investigation, Resources, Validation, Writing – review & editing. Marco Brolese: Investigation, Resources, Validation, Writing – review & editing. Paolo Navalesi: Conceptualization, Methodology, Supervision, Validation, Writing – review & editing. Michele Valmasoni: Conceptualization, Methodology, Investigation, Resources, Supervision, Writing – review & editing. Annalisa Boscolo: Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

All authors made substantial contributions to the conception or design of the work, or to the acquisition, analysis, or interpretation of data; critically revised the manuscript; approved the final version to be published; and agreed to be accountable for all aspects of the work.

Acknowledgements

The authors feel indebted with all the OR and ICU personnel who made this work possible.

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) for English-language editing. The generated text was independently reviewed and verified by the authors, who take full responsibility for the content of the manuscript..

Clinical trial registration

Not applicable. This was a retrospective observational cohort study.

Permission to reproduce material from other sources

Not applicable. The manuscript does not contain previously published material requiring permission for reproduction.

References

1. Coccolini F, Roberts D, Ansaloni L, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* 2018;13:7. doi:10.1186/s13017-018-0167-4
2. Roberts DJ, Leppäniemi A, Tolonen M, et al. The open abdomen in trauma, acute care, and vascular and endovascular surgery: comprehensive, expert, narrative review. *BJS Open.* 2023;7(5):zrad084. doi:10.1093/bjsopen/zrad084
3. García Fernández L. Management of the open abdomen: clinical recommendations for the trauma/acute care surgeon and general surgeon. *Int Wound J.* 2016;13(suppl 3):25–34. doi:10.1111/iwj.12655
4. Camacho Ramirez L, Monasterio CO, Thomas DCJ, et al. Temporary bowel ligation and negative pressure therapy in damage control surgery for the management of septic shock secondary to non-traumatic intestinal perforation. *Cureus.* 2025;17. doi:10.7759/cureus.84374
5. Kirkpatrick AW, Coccolini F, Ansaloni L, et al. Closed Or Open after Source Control Laparotomy for Severe Complicated Intra-Abdominal Sepsis (the COOL trial): study protocol for a randomized controlled trial. *World J Emerg Surg.* 2018;13:26. doi:10.1186/s13017-018-0183-4
6. Kirkpatrick AW, Coccolini F, Tolonen M, et al. The unrestricted global effort to complete the COOL trial. *World J Emerg Surg.* 2023;18. doi:10.1186/s13017-023-00500-z
7. Bleszynski M, Chan T, Buczkowski A. Open abdomen with negative pressure device vs primary abdominal closure for the management of surgical abdominal sepsis: a retrospective review. *Am J Surg.* 2016;211(5):926–932. doi:10.1016/j.amjsurg.2016.01.012
8. Poillucci G, Podda M, Russo G, et al. Open abdomen closure methods for severe abdominal sepsis: a retrospective cohort study. *Eur J Trauma Emerg Surg.* 2021;47. doi:10.1007/s00068-020-01379-0
9. Inukai K, Usui A, Yamada M, et al. Open abdominal management for perforative peritonitis with septic shock: a retrospective analysis on usefulness of a standardized treatment protocol. *Eur J*

- Trauma Emerg Surg. 2021;47:93–98. doi:10.1007/s00068-019-01132-2
10. Prete F, De Luca GD, Pasculli A, et al. Retrospective study of indications and outcomes of open abdomen with negative pressure wound therapy technique for abdominal sepsis in a tertiary referral centre. *Antibiotics (Basel)*. 2022;11(11):1498. doi:10.3390/antibiotics11111498
 11. Shehadeh I, Andrade L, da Silva AILF, et al. Open or closed abdomen post laparotomy to control severe abdominal sepsis: a survival analysis. *Rev Col Bras Cir*. 2024;51:e20243595. doi:10.1590/0100-6991e-20243595-en
 12. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181–1247. doi:10.1007/s00134-021-06506-y
 13. World Union of Wound Healing Societies (WUWHS). Consensus Document: Surgical Wound Dehiscence: Improving Prevention and Outcomes. *Wounds International*; 2018.
 14. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268–281. doi:10.1111/j.1469-0691.2011.03570.x
 15. Li F, Morgan KL, Zaslavsky AM. Balancing covariates via propensity score weighting. *J Am Stat Assoc*. 2018;113(521):390–400. doi:10.1080/01621459.2016.1260466
 16. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702–706. doi:10.1093/aje/kwh090
 17. Royston P, Parmar MKB. Restricted mean survival time: an alternative to the hazard ratio for the design and analysis of randomized trials with a time-to-event outcome. *BMC Med Res Methodol*. 2013;13:152. doi:10.1186/1471-2288-13-152
 18. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: introducing the E-value. *Ann Intern Med* 2017;167(4):268–274. doi:10.7326/M16-2607
 19. White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med*. 2011;30(4):377–399. doi:10.1002/sim.4067
 20. Cirocchi R, Birindelli A, Biffi WL, et al. What is the effectiveness of the negative pressure wound therapy (NPWT) in patients treated with open abdomen technique? A systematic review and meta-analysis. *J Trauma Acute Care Surg*. 2016;81(3):575–584. doi:10.1097/TA.0000000000001126
 21. Kirkpatrick AW, Roberts DJ, Faris P, et al. Active negative pressure peritoneal therapy after abbreviated laparotomy: the Intraperitoneal Vacuum Randomized Controlled Trial. *Ann Surg*. 2015;262(1):38–46. doi:10.1097/SLA.0000000000001095
 22. Cheatham ML, Demetriades D, Fabian TC, et al. Prospective study examining clinical outcomes associated with a negative pressure wound therapy system and Barker's vacuum packing technique. *World J Surg*. 2013;37(9):2018–2030. doi:10.1007/s00268-013-2080-z
 23. Olona C, Caro A, Duque E, et al. Comparative study of open abdomen treatment: ABThera vs abdominal dressing. *Hernia*. 2015;19(2):323–328. doi:10.1007/s10029-014-1253-5

24. Wang G, Xu H, Xu G, Zhang H, Li Z, Liu D. Clinical outcomes of negative pressure wound therapy with instillation vs standard negative pressure wound therapy for wounds: a meta-analysis of randomised controlled trials. *Int Wound J.* 2023;20(5):1739–1749. doi:10.1111/iwj.13989

25. De Pellegrin L, Feltri P, Filardo G, et al. Effects of negative pressure wound therapy with instillation and dwell time versus NPWT or standard of care in orthoplastic surgery: a systematic review and meta-analysis. *Int Wound J.* 2023;20(6):2402–2413. doi:10.1111/iwj.14072

26. Sánchez Betancourt A, Fernández LG. Negative pressure wound therapy with instillation in the septic open abdomen utilizing a modified negative pressure therapy system. *Ann Med Surg (Lond).* 2018;36:246–251. doi:10.1016/j.amsu.2018.10.007

27. Plaudis H, Rudzāts A, Melberga L, Kazaka I, Šuba O, Pupelis G. Abdominal negative-pressure therapy: a new method in countering abdominal compartment and peritonitis - prospective study and critical review of literature. *Ann Intensive Care.* 2012;2(suppl 1):S23. doi:10.1186/2110-5820-2-S1-S23

28. Gasser E, Alexander P, Reich-Weinberger S, et al. Damage control surgery for perforated diverticulitis: a two center experience with two different abdominal negative pressure therapy devices. *Acta Chir Belg.* 2019;119(6):370–375. doi:10.1080/00015458.2018.1534397

Tables

Table 1. Preoperative and decision-time characteristics before and after overlap weighting.

Values are mean (SD) for continuous variables and n (%) for binary/categorical variables before weighting; overlap-weighted columns are weighted means (SDs) or weighted percentages. SMD, standardized mean difference. Because the propensity score was estimated using logistic regression, overlap weighting yields exact finite-sample mean balance for covariates included in the propensity-score model; therefore, post-weighting SMDs for these covariates are expected to approach zero up to numerical precision.

Variable	Missing, <i>n</i>	Unweighted			Overlap-weighted		
		Primary closure	OA- NPWT	SMD	Primary closure	OA- NPWT	SMD
Age, <i>years</i>	0	76.01 (11.93)	72.42 (10.49)	0.322	73.59 (13.46)	73.59 (9.40)	0.000
Female sex, <i>n</i> (%)	0	33 (43.4%)	27 (51.9%)	0.171	51.0%	51.0%	0.000
Body Mass Index, <i>kg/m</i> ²	6	26.87 (6.25)	24.76 (5.35)	0.365	25.07 (4.88)	25.07 (4.76)	0.000
Charlson Comorbidity Index	0	5.75 (2.77)	5.37 (2.48)	0.148	5.47 (2.77)	5.47 (2.54)	0.000
Hospital-to-surgery time, <i>hours</i>	2	59.12 (153.49)	63.09 (234.64)	0.020	68.21 (162.90)	68.21 (232.07)	0.000
Preoperative lactate, <i>mmol/L</i>	19	3.61 (2.50)	5.24 (4.13)	0.481	4.00 (2.51)	4.00 (3.07)	0.000
Preoperative C- reactive protein, <i>mg/L</i>	1	115.02 (128.05)	131.85 (139.40)	0.127	126.52 (125.85)	126.52 (142.59)	0.000
Preoperative SOFA score	1	6.05 (2.24)	6.60 (3.25)	0.196	5.91 (2.13)	5.91 (2.28)	0.000
Preoperative SAPS II	0	51.93 (12.65)	54.00 (15.22)	0.149	51.90 (12.29)	51.90 (10.86)	0.000
Mannheim Peritonitis Index	0	26.29 (6.75)	27.08 (6.63)	0.119	26.77 (7.05)	26.77 (6.10)	0.000
Maximum intraoperative norepinephrine dose, <i>mcg/kg/min</i>	0	0.26 (0.18)	0.32 (0.19)	0.306	0.30 (0.21)	0.30 (0.20)	0.000
Second vasoconstrictor, <i>n</i> (%)	0	1 (1.3%)	12 (23.1%)	0.705	4.5%	4.5%	0.000
Night/holiday operation, <i>n</i> (%)	0	52 (68.4%)	36 (69.2%)	0.017	69.8%	69.8%	0.000
Surgery Type, <i>n</i> (%):							
• upper gastrointestinal	0	13 (17.1%)	0 (0.0%)	0.642	0.0%	0.0%	0.001
• small bowel							
• colorectal or appendiceal	0		22 (42.3%)	0.574	34.7%	34.7%	0.000
• combined or multivisceral	0	13 (17.1%)	21 (40.4%)	0.168	43.4%	43.4%	0.000

0	37 (48.7%)	9 (17.3%)	13 (17.1%)	0.005	21.5%	21.5%	0.000
---	---------------	--------------	---------------	-------	-------	-------	-------

Abbreviations. OA-NPWT, open abdomen with negative-pressure wound therapy.

Table 2. Unadjusted and overlap-weighted clinical outcomes.

For binary outcomes, group estimates are risks, the absolute effect is the risk difference in percentage points (pp), and the relative effect is the risk ratio. For continuous/count outcomes, group estimates are means, the absolute effect is the mean difference, and the relative effect is the ratio of means. The 30-day mortality analysis includes only patients with known day-30 vital status; time-to-event analyses used all patients.

Outcome	Analysis	N	Primary closure	OA-NPWT	Absolute effect (95% CI)	Relative effect (95% CI)
30-day mortality	Unadjusted	120	25.0%	27.1%	2.1 (-14.0 to 18.1) pp	1.08 (0.59 to 2.00)
	Overlap-weighted	120	23.9%	24.8%	0.9 (-18.4 to 20.2) pp	1.04 (0.47 to 2.29)
Abdominal reinterventions	Unadjusted	128	0.11	1.65	1.55 (1.19 to 1.91)	15.71 (7.26 to 33.99)
	Overlap-weighted	128	0.18	1.69	1.51 (1.06 to 1.95)	9.27 (4.04 to 21.27)
Abdominal wound dehiscence	Unadjusted	128	18.4%	11.5%	-6.9 (-19.2 to 5.4) pp	0.63 (0.26 to 1.52)
	Overlap-weighted	128	24.6%	6.5%	-18.1 (-33.6 to -2.6) pp	0.26 (0.08 to 0.82)
MDRO infection	Unadjusted	127	16.0%	11.5%	-4.5 (-16.5 to 7.5) pp	0.72 (0.29 to 1.80)
	Overlap-weighted	127	20.7%	10.3%	-10.4 (-25.9 to 5.1) pp	0.50 (0.17 to 1.42)
CRRT	Unadjusted	128	13.2%	11.5%	-1.6 (-13.2 to 9.9) pp	0.88 (0.34 to 2.26)
	Overlap-weighted	128	13.5%	13.6%	0.2 (-15.3 to 15.6) pp	1.01 (0.32 to 3.18)
Tracheostomy	Unadjusted	128	6.6%	11.5%	5.0 (-5.4 to 15.3) pp	1.75 (0.56 to 5.45)
	Overlap-weighted	128	9.1%	5.3%	-3.8 (-15.4 to 7.8) pp	0.58 (0.12 to 2.74)
Mechanical ventilation days	Unadjusted	126	3.25	6.74	3.48 (1.55 to 5.42)	2.07 (1.33 to 3.22)
	Overlap-weighted	126	3.52	6.29	2.78 (0.60 to 4.96)	1.79 (1.08 to 2.96)
28-day ventilator-free days	Unadjusted	118	19.86	15.38	-4.48 (-8.48 to -0.47)	0.77 (0.61 to 0.98)
	Overlap-weighted	118	19.55	16.23	-3.32 (-8.24 to 1.60)	0.83 (0.63 to 1.10)
ICU length of stay, days	Unadjusted	128	6.09	10.38	4.29 (1.40 to 7.18)	1.70 (1.19 to 2.44)
	Overlap-weighted	128	6.10	9.62	3.53 (-0.17 to 7.22)	1.58 (0.94 to 2.66)

Hospital length of stay, days	Unadjusted	128	19.51	30.71	11.20 (1.41 to 20.99)	1.57 (1.11 to 2.22)
	Overlap-weighted	128	21.92	28.81	6.89 (-3.04 to 16.82)	1.31 (0.89 to 1.95)

Abbreviations. CI, confidence interval. MDRO, multidrug resistant organism. CRRT, continuous renal replacement therapy. ICU, intensive care unit. OA-NPWT, open abdomen with negative-pressure wound therapy.

Table 3. Exploratory effect modification and baseline-risk heterogeneity.

In Panel A continuous modifier risks are ridge-penalized predictions evaluated at the 25th, 50th, and 75th percentiles; interaction p-values are from corresponding robust weighted spline models. NE, not estimable because of sparse treatment-by-modifier cells. For second-vasoconstrictor use, stratum-specific risks and risk differences are ridge-penalized model predictions and are therefore reported despite sparse cells. The formal treatment-by-second-vasoconstrictor interaction test was not estimable because only one primary-closure patient with known 30-day status received a second vasoconstrictor.

Panel B shows overlap-weighted effects by quartile of predicted baseline mortality risk; the continuous treatment-by-risk interaction p-value was 0.898. The optimism-corrected C-statistic of the risk model was 0.746.

Modifier / risk stratum	Evaluation point / range	Risk: primary closure	Risk: OA-NPWT	Risk difference, pp (95% CI)	Interaction p / RR (95% CI)
<i>Panel A. Prespecified individual effect modifiers (25th, 50th, and 75th percentiles)</i>					
Preoperative C-reactive protein	7.77	24.6%	24.9%	0.3 (-0.5 to 1.2)	p=0.752
	57.90	24.6%	24.8%	0.2 (-0.4 to 1.0)	
	214.25	24.2%	24.0%	-0.2 (-0.6 to 0.5)	
Preoperative SOFA score	5.00	24.2%	24.3%	0.1 (-0.3 to 0.6)	p=0.468
	6.00	24.4%	24.4%	0.0 (-0.3 to 0.4)	
	7.00	24.5%	24.5%	-0.0 (-0.4 to 0.3)	
Mannheim Peritonitis Index	22.00	18.1%	18.9%	0.8 (-2.0 to 5.6)	p=0.458
	26.00	20.6%	21.0%	0.5 (-1.7 to 3.8)	
	32.00	28.4%	28.1%	-0.4 (-5.3 to 4.9)	
Maximum intraoperative norepinephrine dose	0.15	21.8%	20.8%	-1.0 (-2.6 to 0.5)	p=0.880
	0.25	22.8%	22.3%	-0.5 (-1.6 to 0.6)	
	0.40	25.1%	26.0%	0.9 (-0.5 to 3.0)	
Operation duration	1.75	24.6%	24.6%	0.0 (-0.6 to 0.8)	p=0.977
	2.38	24.5%	24.5%	0.0 (-0.5 to 0.6)	
	3.06	24.3%	24.3%	0.0 (-0.3 to 0.4)	
Maximum intraoperative lactate	1.73	19.6%	14.3%	-5.3 (-12.5 to 0.7)	p=0.424
	3.17	21.9%	19.3%	-2.6 (-9.4 to 3.5)	

	4.79	25.7%	29.3%	3.7 (-4.3 to 11.5)	
Second vasoconstrictor	No	24.4%	24.4%	0.0 (-0.3 to 0.4)	NE
	Yes	24.3%	24.3%	0.0 (-0.3 to 0.4)	
Panel B. Effect by quartile of predicted baseline mortality risk under primary closure					
Quartile 1	8.5%-15.7%	2.4%	10.5%	8.1 (-13.3 to 29.4)	4.28 (0.26 to 70.70)
Quartile 2	15.9%-21.4%	11.1%	9.4%	-1.6 (-24.2 to 21.0)	0.86 (0.09 to 8.27)
Quartile 3	21.5%-32.0%	27.5%	19.0%	-8.5 (-49.5 to 32.5)	0.69 (0.10 to 4.66)
Quartile 4	32.2%-71.4%	54.8%	61.0%	6.2 (-39.5 to 51.8)	1.11 (0.50 to 2.47)

Abbreviations. OA-NPWT, open abdomen with negative-pressure wound therapy.

Figures

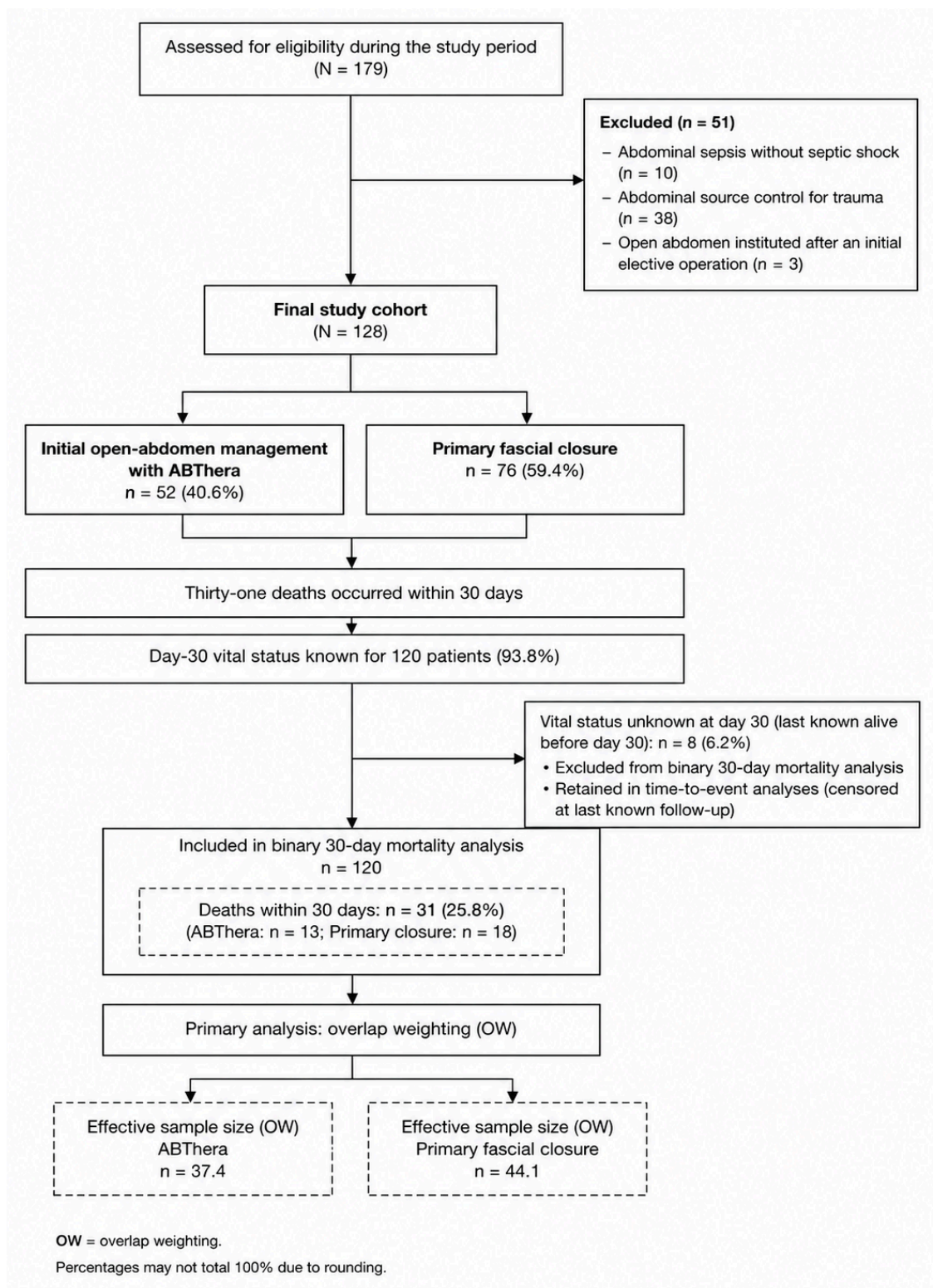


Figure 1

Study flow diagram.

Flow diagram of patient screening, exclusions, final cohort allocation according to the initial abdominal management strategy, ascertainment of 30-day vital status, and effective sample size after propensity-score overlap weighting. Patients without complete 30-day vital status were excluded from the binary mortality analysis but retained in time-to-event analyses with censoring at the last known follow-up.

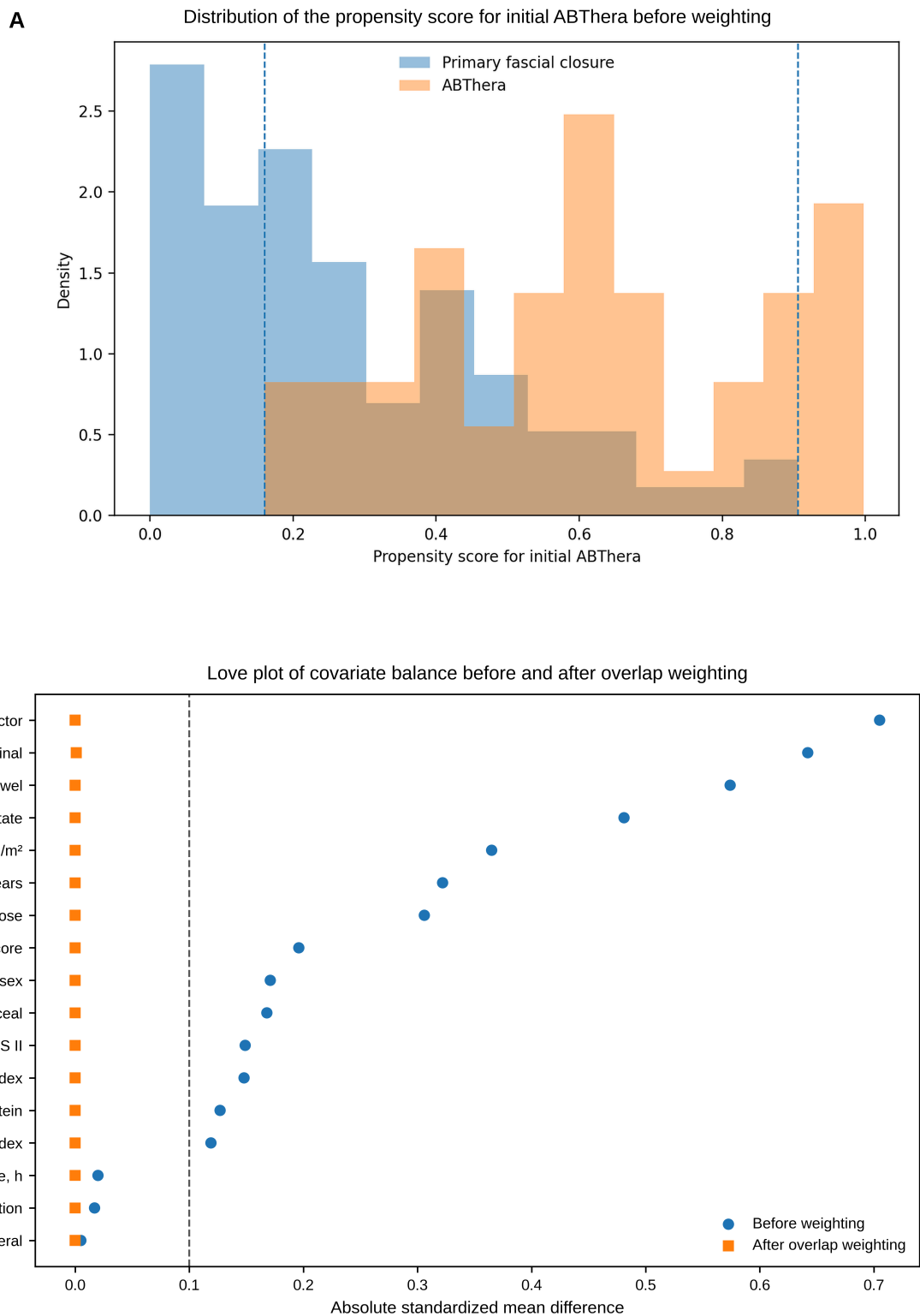


Figure 2

Propensity-score distribution and covariate balance before and after overlap weighting.

(A) Distribution of the propensity score for initial OA-NPWT management before weighting in patients undergoing urgent laparotomy for abdominal septic shock. The dashed vertical lines indicate the lower and upper bounds of the empirical common-support region used in the corresponding sensitivity analysis (0.16 and 0.91, respectively).

(B) Love plot showing absolute standardized mean differences for covariates included in the propensity-score model before and after overlap weighting. Colorectal/appendiceal surgery was the reference category for surgical procedure. The dashed vertical line indicates an absolute standardized mean difference of 0.10. The near-zero post-weighting SMDs reflect the exact finite-sample mean-balance property of logistic-regression-based overlap weights rather than post hoc balance optimization.

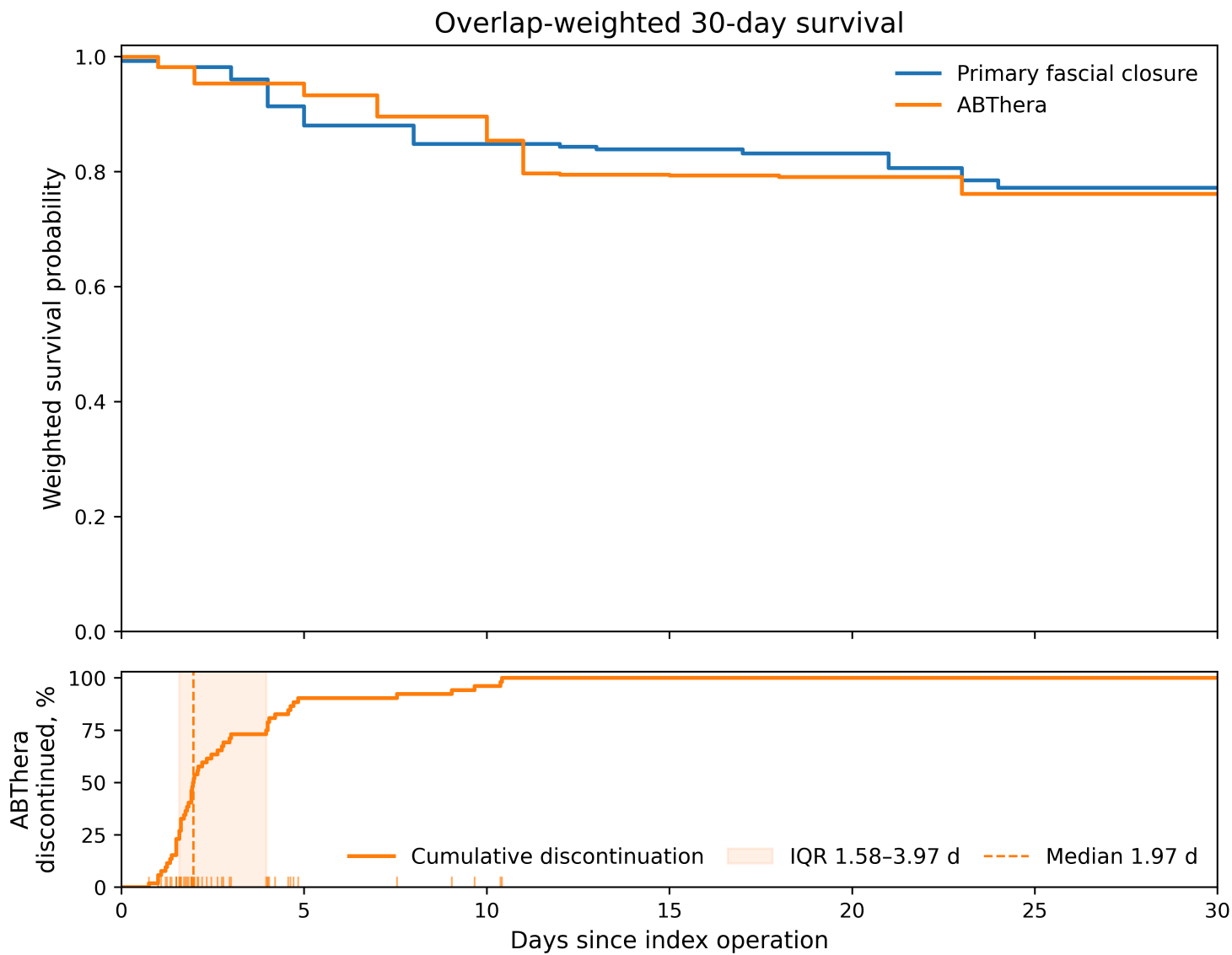


Figure 3

Overlap-weighted 30-day survival according to initial abdominal management strategy.

Upper panel: overlap-weighted Kaplan-Meier survival curves comparing initial open-abdomen management with OA-NPWT and primary fascial closure through 30 days after the index operation. All patients contributed to the time-to-event analysis and were censored at the earlier of last known follow-up or day 30. Overlap-weighted cumulative 30-day mortality was 23.9% with OA-NPWTa and 22.8% with primary fascial closure. Restricted mean survival time through day 30 was 25.09 versus 25.42 days, respectively, corresponding to a difference of -0.33 days (95% bootstrap CI, -4.44 to 3.61).

Lower panel: descriptive empirical cumulative distribution of the recorded duration of OA-NPWT placement among the 52 patients initially managed with OA-NPWT. Rug marks indicate individual patient durations; the dashed vertical line indicates the median duration (1.97 days), and the shaded area indicates the interquartile range (1.58–3.97 days). The lower panel is unweighted and descriptive and should not be interpreted as a time-varying treatment-effect analysis.

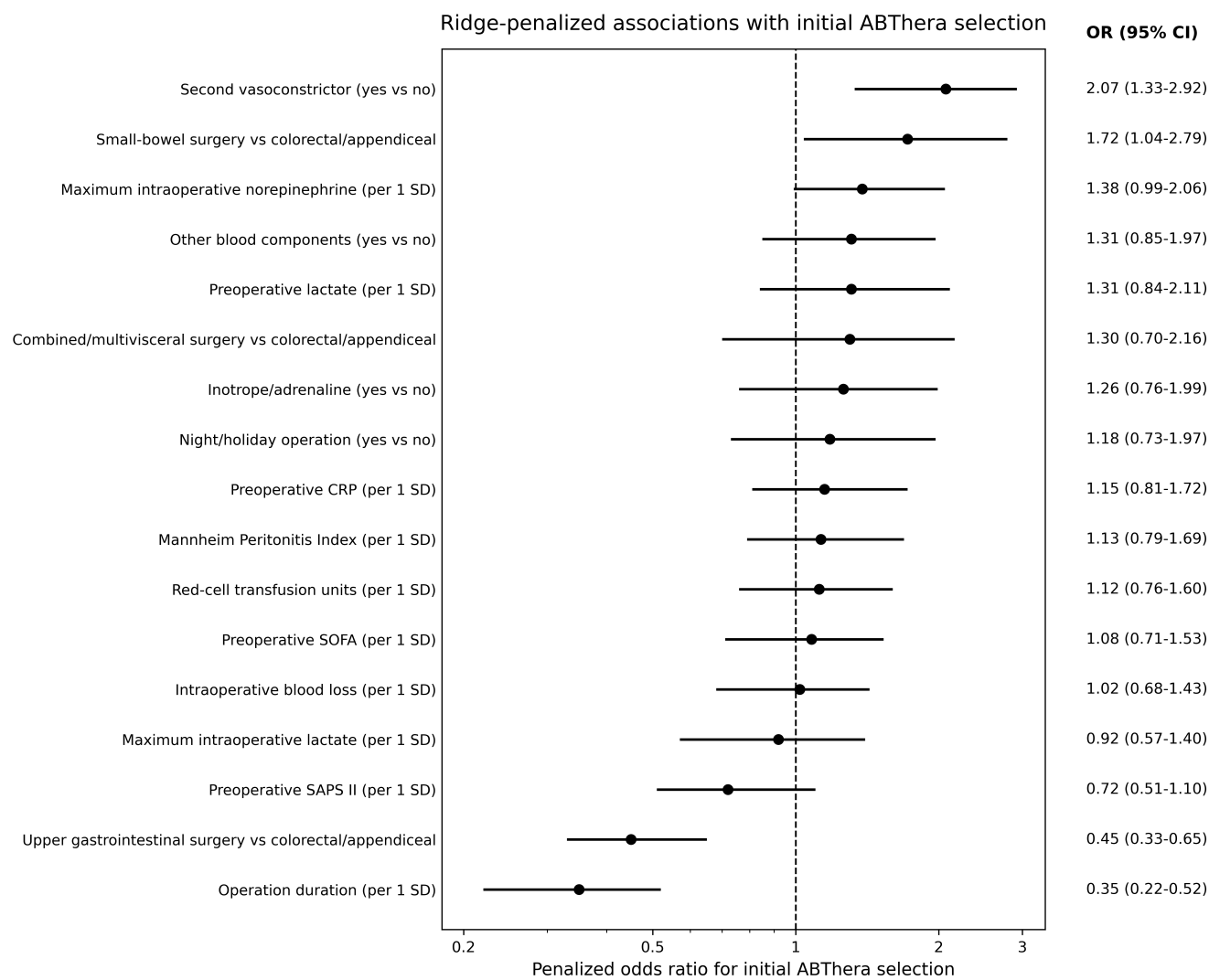


Figure 4

Ridge-penalized associations with selection of initial OA-NPWT management.
 Forest plot of odds ratios and 95% bootstrap confidence intervals from the ridge-penalized logistic regression model evaluating factors associated with initial OA-NPWT selection. Continuous predictors are expressed per 1-SD increase; categorical predictors are expressed relative to the indicated reference category. Colorectal/appendiceal surgery was the reference surgical category. Estimates describe treatment-selection associations and should not be interpreted as treatment effects.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [AbtheraSupplTables.docx](#)
- [AbtheraSupplMethods.docx](#)
- [AbtheraSupplFig.docx](#)