Treatments and other prognostic factors in the management of the open abdomen: A systematic review

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BACKGROUND: The open abdomen (OA) is an important approach for managing intra-abdominal catastrophes and continues to be the standard of care. Despite this, challenges remain with it associated with a high incidence of complications and poor outcomes. The objective of this article is to perform a systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to identify prognostic factors in OA patients in regard to definitive fascial closure (DFC), mortality and intra-abdominal complications.

METHODS: An electronic database search was conducted involving Medline, Excerpta Medica, Central Register of Controlled Trials, Cumulative Index to Nursing, and Allied Health Literature and Clinicaltrials.gov. All studies that described prognostic factors in regard to the above outcomes in OA patients were eligible for inclusion. Data collected were synthesized by each outcome of interest and assessed for methodological quality.

RESULTS: Thirty-one studies were included in the final synthesis. Enteral nutrition, organ dysfunction, local and systemic infection, number of reexplorations, worsening Injury Severity Score, and the development of a fistula appeared to significantly delay DFC. Age and Adult Physiology And Chronic Health Evaluation version II score were predictors for in-hospital mortality. Failed DFC, large bowel resection and >5 to 10 L of intravenous fluids in <48 hours were predictors of enteroatmospheric fistula. The source of infection (small bowel as opposed to colon) was a predictor for ventral hernia. Large bowel resection, >5 to 10 and >10 L of intravenous fluids in <48 hours were predictors of intra-abdominal abscess. Fascial closure on (or after) day 5 and having a bowel anastomosis were predictors for anastomotic leak. Overall methodological quality was of a moderate level.

LIMITATIONS: Overall methodological quality, high number of retrospective studies, low reporting of prognostic factors and the multitude of factors potentially affecting patient outcome that were not analyzed.

CONCLUSION: Careful selection and management of OA patients will avoid prolonged treatment and facilitate early DFC. Future research should focus on the development of a prognostic model. (*J Trauma Acute Care Surg.* 2017;82: 407–418. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Systematic review, level III.

KEY WORDS: Risk factors; open abdomen; laparostomy; regression; predictors.

The open abdomen (OA) is an important approach for managing intra-abdominal catastrophes and continues to be the standard of care.[1] Despite this, challenges remain and the technique is still associated with a high incidence of complications and poor outcomes.[2]

Currently, there are no published reviews (collective or systematic) of prognostic factors in regard to definitive fascial closure (DFC), mortality, and intra-abdominal complications of patients being managed with an OA. There are, however, some factors associated with the development of these outcomes in patients managed with an OA that have been noted in recent publications. For example, the presence of multiorgan failure and ongoing sepsis is associated with delaying DFC, whereas diverticulitis is associated with development of enteroatmospheric fistula in the OA.[3–5] Early DFC of the abdomen (<7 days after initial laparotomy) is also a factor that has been shown to significantly improve survival in patients being managed with an OA.[6]

Assessing a patient's risk of mortality and likelihood of developing these complications would therefore aid in their safe and timely management and provide the ability to plan subsequent interventions until DFC can be achieved.

The objective of this study was to systematically review the literature on the management of patients with an OA to identify prognostic factors related to DFC, mortality, and intra-abdominal complications.

METHODS

This systematic review was performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline.[7] The protocol for this systematic review was registered on PROSPERO (CRD42015019343) and is available in full on their website.[8]

Eligibility Criteria

All studies that included hospitalized patients, aged 18 years or older, who underwent laparotomy, regardless of indication or sex, and were unable to have primary fascial closure completed at the end of their initial operation necessitating temporary abdominal closure were eligible for inclusion. Prognostic factors included those for DFC, perioperative (death within 30 days of initial laparostomy) and in-hospital mortality (death within the patient's index admission), and/or intra-abdominal complications (enteroatmospheric fistula, abscess, ventral hernia, and anastomotic leak). All peer-reviewed publications and unpublished studies (randomized-controlled trials, retrospective, prospective, observational cohort and case series with five or more patients) were considered.

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TABLE 1. Search Terms Used in Systematic Review

MeSH	Not used
Free text words	risk AND factors AND open AND abdomen
	risk AND factors AND laparostomy
	regression AND open AND abdomen
	predictors AND open AND abdomen
Field	All fields
Limits	None

MeSH, medical subject headings.

Literature Search

A systematic literature search was performed of the following electronic databases: Medline (PubMed), EMBASE (Ovid), Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature, and Clinicaltrials.gov. No restrictions were placed in regard to language or publication date, with dates of coverage including from January 1, 1950, up until a final search was performed on January 9, 2016. Reference lists of all included studies and relevant review articles were searched manually for additional relevant articles. Unpublished data from relevant trials were also requested from the corresponding authors as necessary by letters or electronic mail. The search strategy was constructed in consultation with a senior staff librarian. Two of the authors (A.C. and S.J.) independently searched the above databases using key words related to prognostic factors in the management of the OA (Table 1). Titles, followed by abstracts and then full-text articles were retrieved and read by both authors and were further assessed for relevance before inclusion into the systematic review. Handsearching of electronic links to related articles and references of included studies was also performed. Disagreement on relevance was addressed firstly by discussion and consensus among the two authors involved in the data extraction (A.C. and S.J.). Failing this, disagreements were then resolved by a consensus meeting with a third author (K.H.).

Study Selection

Screening, eligibility and inclusion of studies in the systematic review was performed by two authors independently (A.C. and S.J.).[7] All published and unpublished studies that included prognostic factors identified in the management of the OA (regardless of etiology). Specific study inclusion and exclusion criteria are detailed in Table 2.

Data Extraction

Data were collected independently by two authors (A.C. and S.J.) using an electronic database.[7] Investigators of included studies were contacted to confirm data that were unclear, also to obtain further data that were not available from the original article. The collected data included study characteristics (first author, publication year, design, regression method), patient characteristics (number of patients, age, indication for OA), overall percentage of patients in regard DFC,intra-abdominal complications (enteroatmospheric fistula, ventral hernia, abscess, anastomotic leak), and/or mortality (perioperative, in-hospital), as well as characteristics of relevant prognostic factors (prognostic factor, odds or hazard ratio with 95% confidence intervals, p value). Results from univariate and multivariate models were reported separately. When series of multivariate models were present in studies, the results of the most adjusted model were chosen.

Methodological Quality

A risk of bias assessment was performed individually for the list of included studies using the nine-item Newcastle-Ottawa quality assessment scale for case-control and cohort studies.[9] Methodological components assessed included: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively. The median and interquartile range were then calculated to provide an overall assessment of methodological quality across the included studies. Authors again resolved disagreements by discussion and consensus, with involvement of a third author, if required (K.H.).

RESULTS

Study Selection

The initial database search identified 978 studies (Fig. 1). This included 493 studies from Medline, 269 studies from EMBASE, 27 studies from Cochrane Central Register of Controlled Trials, 43 studies from Cumulative Index to Nursing and Allied Health Literature, and 146 studies from the clinicaltrials.gov website. A further 146 studies were identified from the reference lists of included studies. Two hundred forty-seven of these were identified as duplicate studies and subsequently excluded. Systematic exclusions were then made, leaving a total of 31 studies in the final review.[10–40] Sixteen studies were excluded in the final stages (full-text) of the systematic review.[41–56] This was due to the studies reporting on prognostic factors in regard to outcomes that were not considered in this review (e.g., adult respiratory distress syndrome; eight studies),[41–48] studies that identified significant prognostic factors using statistical methods other than regression (e.g., χ^2; seven studies)[49–55] or prognostic factors that were in regard to the outcomes of interest, but the results were not significant (one study).[56]

TABLE 2. Study Inclusion and Exclusion Criteria

Inclusion criteria	• Studies presenting own original data from at least five patients over the age of 18 y
	• Studies including prognostic factors in regard to at least one of the outcomes:
	○ DFC
	○ Mortality, or
	○ Intra-abdominal complications (enteroatmospheric fistula ventral hernia, abscess, and anastomotic leak)
	• Studies that reported on the same population, but published different prognostic factors
	• Studies that used regression methods for statistical analyses and reported odds ratios or hazards ratios
Exclusion criteria	• Studies that were reviews (systematic or critical), letters to the editor, editorials or non-peer reviewed articles

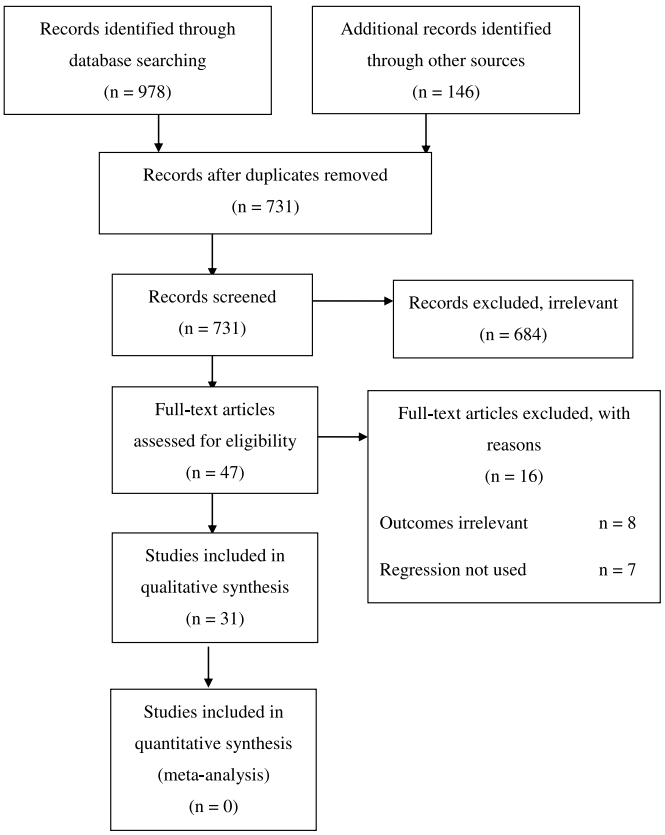

Figure 1. PRISMA 2009 flow diagram showing study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[7]

Study Characteristic and Results of Individual Studies

The 31 included studies were published from 1996 to 2015 and involved a total of 6,989 patients, with mean age of 47 ± 15 years. Prognostic factors for DFC were most frequently reported (15 studies),[10,13,14,18,24–26,28,31,35–40] followed by those for in-hospital mortality (12 studies),[10–12,18,20–22,27,30–33] anastomotic leak (three studies),[17,29,34] perioperative mortality,[19,23] enteroatmospheric fistula,[15,38] ventral hernia,[16,29] and abscess[15,29] (two studies each). Twenty-two studies had a retrospective case-control design,[11,13,14,16–18,21–23,25,27–34,36,37,39,40] eight studies had a prospective cohort design,[10,15,19,20,24,26,35,38] and one study had components of both study designs.[12] None of the included studies were randomized-controlled trials. Characteristics and outcomes of individual studies are shown in Tables 3, 4, and 5.

There were various indications for patients being managed with an OA. Trauma was the most frequent (22 studies),[10–13,15–19,22–24,26,28,29,31,32,34,35,37–39] followed by peritonitis (intra-abdominal sepsis; 14 studies),[10,11,14,16,19,21,22,25,27,30,31,33,38,40] abdominal compartment syndrome (intra-abdominal hypertension; seven studies),[11,14,20,27,31,32,39] vascular emergencies (five studies),[10,11,25,27,36] ischemic bowel (two studies),[16,31] and pancreatitis (one study).[36]

Risk of Bias Within and Across Studies

After risk of bias assessment of the 31 included studies using the Newcastle-Ottawa scale quality assessment score, 18 studies scored 3 points,[11,15–18,20–25,27–29,32,33,35,39] three studies scored 4 points,[30,34,40] and 10 studies scored 5 points,[10,12–14,19,26,31,36–38] out of a possible score of 9. The median score was 3 (interquartile range: 3–5), which demonstrates that the overall methodological quality of the included studies was of a moderate level.

For case-control studies, selection of controls, comparability of cases and controls on the basis of the design or analysis, ascertainment of exposure and same method of ascertainment for cases and controls were reported particularly well. For cohort studies, ascertainment of exposure, demonstration that outcome of interest was not present at start of study and assessment of outcome were reported particularly well. Selection of the nonexposed cohort or controls and adequacy of follow-up were reported particularly poorly among both study designs.

In regard to publications bias, all included studies were from published data because no relevant unpublished data were found in the literature search.

Synthesis of Results

DFC rates were reported in 15 of the included studies. Of the prognostic factors identified, enteral nutrition (two studies), organ dysfunction (three studies), local and systemic infection (five studies), number of reexplorations (three studies), Injury Severity Score (ISS) (three studies) and the development of a fistula (three studies) appeared most often in regard to delaying DFC.[10,13,18,24,31,35–40] Odds ratios for enteral nutrition ranged between 0.18 and 0.48, 2.3 and 5.1 for organ dysfunction, 2.1 and 17 for local and systemic infection, 1.3 and 5.6 for number of reexplorations, 0.94 and 2.5 for ISS (when ISS > 15), and 6.4 and 8.6 for fistula. Further prognostic factors in regard to delaying DFC are detailed in Table 3.

Perioperative mortality was reported in two studies. The prognostic factors identified appeared to protect against perioperative mortality, as opposed to influencing it. Regardless, the use of ≥48 hours of ABThera of Negative Pressure Wound Therapy (as opposed to Baker's Vacuum Packing Technique; odds ratio [OR], 0.31; 95% confidence interval [CI], 0.12–0.83) and the use of a protocol for damage control resuscitation (OR, 0.40; 95% CI, 0.18–0.91) were identified in regard to perioperative mortality.[19,23]

In-hospital mortality was reported in 12 studies. Of the prognostic factors identified, age (six studies) and Adult Physiology And Chronic Health Evaluation version II (APACHE II) score (four studies) appeared most often in regard to in-hospital mortality.[10,12,20,22,27,30,32,33] Odds ratios for age ranged between 0.18 and 1.2, whereas for APACHE II score, they ranged from 1.1 to 3.0 (APACHE II score, ≥25). Further prognostic factors in regard to mortality are detailed in Table 4.

Enteroatmospheric fistula was reported in two studies. Failed DFC (OR, 7.5; 95% CI, 1.2–46), large bowel resection (performed while a patient was being managed with an OA; OR, 3.56; 95% CI, 1.88–6.76) and total fluid intake at 48 hours of 5 to 10 L (OR, 2.11; 95% CI, 1.15–3.88) were identified as the prognostic factors in regard to the development of an enteroatmospheric fistula.[15,38]

Ventral hernia was reported in two studies. The source of infection (small bowel in relation to colon; OR, 1.7; 95% CI,

TABLE 3. Prognostic Factors for Delaying DFC

Study Name	Year	Study Design	N	Age*	Indication for OA	% Fascial Closure	QAS score	Regression Method	Prognostic Factor	OR (95% CI)	*p*
Acosta et al.[10]	2011	Prospective, cohort	111	68 (20–91)	Trauma peritonitis vascular	77	5	Multivariate binary logistic	Intestinal fistula	8.6 (1.5–50)	0.017
Beale et al.[13]	2013	Retrospective, case-control	62	35 ± 16	Trauma	71	5	Univariate binary logistic	Increasing Penetrating Abdominal Trauma Index score	1.1 (1.0–1.1)	<0.05
									Worsening base excess on arrival	0.79 (0.66–0.93)	<0.05
									Lower ISS	0.94 (0.89–1.0)	<0.05
Bertelsen et al.[14]	2014	Retrospective, case-control	101	67 (61–74)	ACS peritonitis	66	5	Multivariate Cox	Indication for OA—peritonitis	2.0 (1.1–3.5)**	0.022
									Indication for OA—failure of fascial closure	4.7 (2.2–10) **	<0.001
									Indication for OA—fascial necrosis	9.7 (1.3–73) **	0.027
									Stoma during OA	2.0 (1.1–3.6)**	0.019
Burlew et al.[18]	2012	Retrospective, case-control	597	38 ± 1	Trauma	70	3	Multivariate binary logistic	Enteral nutrition without bowel injury	0.189 (N/A)	<0.01
									Enteral nutrition with blunt trauma vs. penetrating trauma	0.345 (N/A)	<0.01
									Enteral nutrition vs. nil per oral	0.476 (N/A)	<0.01
DuBose et al.[24]	2013	Prospective, cohort	572	39 ± 17	Trauma	59	3	Multivariate binary logistic	No. reexplorations required	1.34 (1.15–1.57)	<0.001
									Development of intra-abdominal abscess/sepsis	2.43 (1.22–4.83)	0.011
									Development of blood stream infection	2.60 (1.18–5.70)	0.017
									Development of acute renal failure	2.31 (1.19–4.46)	0.013
									Development of enteric fistula	6.38 (1.23–32.9)	0.027
									ISS > 15	2.48 (1.06–5.85)	0.037
Frazee et al.[25]	2013	Retrospective, case-control	74	51 (7–84)	Peritonitis vascular	74	3	Multivariate binary logistic	ABThera NPWT vs. BVPT	0.13 (0.03–0.50)	<0.05
Glaser et al.[26]	2015	Prospective, cohort	172	24 ± 5	Trauma	96	5	Multivariate binary logistic	Ratio-driven resuscitation	0.36 (0.19–0.69)	<0.05
Hatch et al.[28]	2011	Retrospective, case-control	282	35 (25–47)	Trauma	65	3	Multivariate binary logistic	Vacuum-assisted closure used at initial laparotomy	0.32 (0.15–0.71)	0.006
									Intensive care unit international normalised ratio	5.6 (1.0–29)	0.016
									Intensive care unit peak intra-arterial pressure, mm Hg	1.2 (1.1–1.3)	0.004
Kafka-Ritsch et al.[31]	2012	Retrospective, case-control	160	66 (21–88)	Trauma ACS peritonitis ischemia	76	5	Multivariate binary logistic	Female sex	0.37 (0.16–0.86)	0.02
									Limited surgery	N/A (N/A)	0.02
									Generalized peritonitis	N/A (N/A)	0.05

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TABLE 3. *(Continued)*

Study Name	Year	Study Design	N	Age*	Indication for OA	% Fascial Closure	QAS score	Regression Method	Prognostic Factor	OR (95% CI)	*p*
Pommerening et al.[35]	2014	Prospective, cohort	499	36 (23–51)	Trauma	66	3	Multivariate binary logistic	Time to take back	1.0 (1.0–1.0)	0.045
									24-h crystalloids > 10 L	2.0 (1.1–3.6)	0.032
									No. take-backs	5.6 (3.4–9.1)	<0.001
									ISS > 15 + Bowel resection	1.7 (1.0–2.9)	0.04
Rasilainen et al.[36]	2012	Retrospective, case-control	50	60 (24–83)	Pancreatitis; vascular	78	5	Multivariate binary logistic	Vacuum-assisted closure and MeSH-mediated fascial traction	0.23 (0.08–0.63)	<0.05
									Miscellaneous diagnosis†	0.29 (0.09–0.91)	<0.05
									Renal dysfunction	2.7 (1.0–7.1)	<0.05
									Indication for OA—Intra-abdominal hypertension or prophylactic	0.34 (0.09–1.4)	<0.05
Riha et al.[37]	2011	Retrospective, case-control	71	26 ± 7	Trauma	65	5	Multivariate ordinal logistic	Massive transfusion	3.9 (N/A)	<0.05
									Presence of complications	5.1 (N/A)	<0.05
									Injury date in 2005 vs. 2006	3.4 (N/A)	<0.05
Teixeira et al.[38]	2008	Prospective, cohort	93	33 ± 15	Trauma peritonitis	85	5	Multivariate binary logistic	Presence of deep surgical site infection	17 (2.6–116)	0.003
									Presence of intra-abdominal abscess	7.4 (1.1–51)	0.04
Vogel et al.[39]	2006	Retrospective, case-control	344	36 ± 16	Trauma ACS	52	3	Multivariate binary logistic	Blood stream infection	2.1 (1.2–3.8)	0.01
									Surgical site infection	2.9 (1.5–5.6)	<0.01
									Packed red blood cells > 21 units	3.1 (1.7–5.6)	<0.01
Yuan et al.[40]	2013	Retrospective, case-control	72	44 (19–83)	Peritonitis	49	4	Multivariate binary logistic	Modified sandwich-vacuum package	0.20 (0.06–0.67)	0.008
									Early enteral nutrition (<1 wk of hospital admission)	0.18 (0.05–0.59)	0.006

N, number of patients; ACS, Abdominal Compartment Syndrome; QAS, Newcastle-Ottawa Scale Quality Assessment Scale; NPWT, Negative Pressure Wound Therapy; BVPT, Baker's Vacuum Packing Technique; N/A, not available in article data.

*All diagnoses other than acute pancreatitis, ruptured abdominal aortic aneurysm or peritonitis.

**Hazard ratio.

†Age either reported as mean ± SD or median (range), where applicable.

TABLE 4. Prognostic Factors for Mortality

Mortality	Study Name	Year	Study Design	N	Age*	Indication for OA	% Mortality	QAS Score	Regression Method	Prognostic Factor	OR (95% CI)	*p*
Perioperative	Cheatham et al.[19]	2013	Prospective, cohort	280	40 ± 16	Trauma peritonitis	15	5	Multivariate binary logistic	≥48 hours of ABThera™ NPWT vs. BVPT	0.31 (0.12–0.83)	0.02
	Cotton et al.[23]	2011	Retrospective, case-control	390	35 (24–47)	Trauma	21	3	Multivariate binary logistic	Damage control resuscitation	0.40 (0.18–0.91)	0.028
										Emergency department arrival base value	0.91 (0.83–1.0)	0.011
In-hospital	Acosta et al.[10]	2011	Prospective, cohort	111	68 (20–91)	Trauma peritonitis vascular	30	5	Multivariate binary logistic	Age	1.2 (1.0–1.4)	0.027
										Failure of fascial closure	45 (1.1–1.7 × 10^3)	0.043
	Arhinful et al.[11]	2011	Retrospective, case-control	67	84 (80–98)	Trauma ACS peritonitis vascular	37	3	Multivariate binary logistic	Acute renal failure	12 (2.0–69)	0.006
										Congestive heart failure	11 (1.0–1.3 × 10^2)	0.029
	Asensio et al.[12]	2004	Retrospective, case-control/ Prospective, cohort	139	33 ± 14	Trauma	25	5	Multivariate binary logistic	Age <55 y	0.18 (0.05–0.56)	<0.001
										Organ failure	3.3 (1.4–10)	0.04
										Infection	0.34 (0.13–0.91)	0.03
	Burlew et al.[18]	2012	Retrospective, case-control	597	38 ± 1	Trauma	14	3	Multivariate binary logistic	Enteral nutrition without bowel injury	0.300 (N/A)	0.01
										Enteral nutrition with blunt trauma vs. penetrating trauma	0.310 (N/A)	<0.01
										Enteral nutrition vs. nil per oral	0.400 (N/A)	0.01
	Cheatham and Safcsak[20]	2010	Prospective, cohort	478	43 ± 18	ACS	40	3	Multivariate binary logistic	ACS	5.6 (2.7–11)	<0.001
										Prophylactic OA	0.31 (0.17–0.56)	<0.001
										APACHE II score ≥ 25	3.0 (1.6–5.6)	0.001
										Study year	1.2 (1.0–1.3)	0.018
	Chiarugi et al.[21]	2011	Retrospective, case-control	52	67 (15–94)	Peritonitis	38	3	Multivariate binary logistic	Mannheim Peritonitis Index	N/A (N/A)	<0.05
	Clark et al.[22]	2013	Retrospective, case-control	720	44 ± 19	Trauma ACS peritonitis	38	3	Multivariate binary logistic	Age	1.03 (1.01–1.04)	<0.001
										APACHE II Score	1.14 (1.09–1.18)	<0.001
										ISS	1.04 (1.02–1.06)	<0.001
										Self-pay (uninsured)	2.84 (1.51–5.35)	0.001

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TABLE 4. *(Continued)*

Mortality	Study Name	Year	Study Design	N	Age*	Indication for OA	% Mortality	QAS Score	Regression Method	Prognostic Factor	OR (95% CI)	*p*
In-hospital (cont…)	Grunau et al.[27]	1996	Retrospective, case-control	48	58 (20–95)	Peritonitis vascular	38	3	Multivariate ordinal logistic	APACHE II Score	N/A (N/A)	<0.05
										Mannheim Peritonitis Index	N/A (N/A)	<0.05
										Age	N/A (N/A)	<0.05
										Glasgow Coma Scale	N/A (N/A)	<0.05
										Chronic Health Evaluation	N/A (N/A)	<0.05
	Holzheimer and Gathof[30]	2003	Retrospective, case-control	145	57 ± 18	Peritonitis	30	4	Multivariate ordinal logistic	Abdominal closure	N/A (N/A)	<0.001
										Haemorrhage	N/A (N/A)	0.003
										Pneumonia	N/A (N/A)	0.015
										Insufficiency	N/A (N/A)	0.029
										Translocation	N/A (N/A)	0.044
										Liver	N/A (N/A)	0.031
										Multiple Organ Failure score	N/A (N/A)	<0.001
										APACHE II	N/A (N/A)	<0.001
										Multiple Organ Dysfunction Score	N/A (N/A)	<0.001
	Kafka-Ritsch et al.[31]	2012	Retrospective, case-control	160	66 (21–88)	Trauma ACS peritonitis ischemia	21	5	Multivariate binary logistic	Male sex	N/A (N/A)	0.05
										Mannheim Peritonitis Index > 25	N/A (N/A)	0.02
										Extensive surgery	N/A (N/A)	0.03
	Montalvo et al.[32]	2005	Retrospective, case-control	120	36 ± 14	Trauma ACS	59	3	Multivariate binary logistic	Average age	1.1 (N/A)	0.037
										Initial base deficit	0.90 (N/A)	0.01
	Mulier et al.[33]	2003	Retrospective, case-control	96	57 ± 15	Peritonitis	30	3	Multivariate ordinal logistic	Failed clearance of abdomen (including failed control of septic source)	7.7×10^4 $(10 - +\infty)$**	<0.001
										Age	1.1 (1.1–1.2)	<0.001
										Unconsciousness	12 (1.5–1.4 × 10^2)	0.013

*Because all patients without control of the septic source also lacked clearance of the abdomen, the effect of control of the septic source could not be estimated independently.
**Age either reported as mean ± SD or median (range), where applicable.

TABLE 5. Prognostic Factors for Intra-Abdominal Complications

Complication	Study Name	Year	Study Design	N	Age*	Indication for OA	% Complication	QAS score	Regression Method	Prognostic Factor	OR (95% CI)	p
Enteroatmospheric fistula	Bradley et al.[15]	2013	Prospective, cohort	517	39 ± 17	Trauma	22*	3	Multivariate binary logistic	Large bowel resection	3.56 (1.88–6.76)	<0.001
										Total fluid intake at 48 hours: 5–10 L	2.11 (1.15–3.88)	0.02
										Total fluid intake at 48 hours: >10 L	1.93 (1.04–3.57)	0.04
										Number of re-explorations	1.14 (1.06–1.21)	<0.001
	Teixeira et al.[38]	2008	Prospective, cohort	93	33 ± 15	Trauma peritonitis	15	5	Multivariate binary logistic	Failed DFC	7.5 (1.2–46)	0.03
Ventral hernia	Brandl et al.[16]	2014	Retrospective, case-control	112	63 (16–92)	Trauma peritonitis ischemia	35	3	Univariate binary logistic	Source of infection: Small bowel infection (as opposed to colon)	1.7 (N/A)	0.04
	Hatch et al.[29]	2011	Retrospective, case-control	282	35 (25–47)	Trauma	9	3	Multivariate binary logistic	Closed at initial take back	0.31 (0.13–0.72)	0.007
Abscess	Bradley et al.[15]	2013	Prospective, cohort	517	39 ± 17	Trauma	22*	3	Multivariate binary logistic	Large bowel resection	3.56 (1.88–6.76)	<0.001
										Total fluid intake at 48 hours: 5–10 L	2.11 (1.15–3.88)	0.02
										Total fluid intake at 48 hours: > 10 L	1.93 (1.04–3.57)	0.04
										Number of re-explorations	1.14 (1.06–1.21)	<0.001
	Hatch et al.[29]	2011	Retrospective, case-control	282	35 (25–47)	Trauma	22	3	Multivariate binary logistic	Closed at initial take back	0.28 (0.12–0.66)	0.004
Anastomotic leak	Burlew et al.[17]	2011	Retrospective, case-control	204	37 ± 1	Trauma	7	3	Multivariate binary logistic	Fascial closure on day 5 or after	4.1 (1.0–5.0)	0.02
	Hatch et al.[29]	2011	Retrospective, case-control	282	35 (25–47)	Trauma	4	3	Multivariate binary logistic	ISS	0.96 (0.93–0.98)	0.006
										Closed at initial take back	0.23 (0.09–0.56)	0.001
	Ott et al.[34]	2011	Retrospective, case-control	79	37 (28–48)	Trauma	15	4	Multivariate binary logistic	Having an anastomosis	6.4 (N/A)	0.002

*Enterocutaneous fistula, enteroatmospheric fistula and intra-abdominal sepsis/abscess were grouped together in this study.

not available) was the only prognostic factor identified in regard to the development of a ventral hernia.[16]

Intra-abdominal abscess was reported in two studies. Large bowel resection (performed while a patient was being managed with an OA; OR, 3.56; 95% CI, 1.88–6.76) and total fluid intake at 48 hours of 5 to 10 L (OR, 2.11; 95% CI, 1.15–3.88) and >10 L (OR, 1.93; 95% CI, 1.04–3.57) were identified as the prognostic factors in regard to the development of an intra-abdominal abscess.[15]

Anastomotic leak was reported in three studies. Having an anastomosis (OR, 6.4; 95% CI, not available) and fascial closure on day 5 or after (OR, 4.1; 95% CI, 1.0–5.0) were the only two prognostic factors identified in regard to the development of an anastomotic leak.[17,34] Further prognostic factors in regard to intra-abdominal complications are detailed in Table 5.

DISCUSSION

Summary of Evidence

This systematic review provides an extensive overview of prognostic factors in OA patients in regard to DFC, mortality, and intra-abdominal complications.

Prognostic factors for DFC were most frequently reported. Enteral nutrition, organ dysfunction, local and systemic infection, number of reexplorations, worsening ISS, and the development of a fistula appeared to significantly delay DFC. This shows that intra-abdominal complications, especially infective, that develop while a patient is being managed with an OA can significantly affect the ability to achieve early DFC.[55]

Age and APACHE II score were significantly prognostic in regard to in-hospital mortality. This reflects the severe nature of the OA and the need for early involvement of a multidisciplinary team. Careful selection of patients to be managed with an OA therefore needs to be done to avoid prolonged OA treatment.[55]

Large bowel resection, large administration of intravenous fluids (>5–10 L) in the early postoperative period (<48 hours) and an increased number of re-operations appears to influence the development of enteroatmospheric fistula and abscess. The source of infection (small bowel as opposed to colon) appeared to influence the development of ventral hernias. Although delayed DFC (>5 days) and the presence of a bowel anastomosis appeared to influence the development of an anastomotic leak. This again shows how ongoing infections can affect patient outcomes. Contaminated OA patients often have increased transfusion requirements, use a greater amount of health resources, and hence have an increased number of infectious complications.[15,27,48]

Prognostic factors identified in this systematic review will aid in avoiding prolonged treatment and facilitate better outcomes in OA patients. Unfortunately, there are currently no prognostic models, calculators, probability nomograms, or scoring systems in regard to these outcomes for use in current clinical practice.

Strengths and Limitations

This is the first systematic review of prognostic factors in the management of the OA. The results of this article provide the basis for future research in the field of OA management. Subsequent development of a prognostic model that could be used to not only predict the likelihood of complications and mortality but also highlight certain aspects of treatment which could be modified such to improve patient outcomes.

There are, however, a few limitations associated with this systematic review, chiefly regarding methodological quality and study design of the included studies. The overall methodological quality of the included studies was of a moderate level. There were no randomized-controlled trials within the included studies. This means that the level of evidence behind conclusions drawn from this systematic review is not high. The study design of the included studies consisted of 22 studies being retrospective case-control and seven studies being prospective cohort, with one study having components of both study designs. With the majority of the included studies being of a retrospective nature from published literature, confounding and/or publication bias and heterogeneity have almost certainly influenced these results. All future studies should provide conclusive data about prognostic factors in regard to predicting patient outcome in the management of their OA.

Another potential limitation was the low incidence of prognostic factors being reported in regard to outcomes in the included studies, as well as the multitude of confounding factors that could potentially influence patient outcome while being managed with an OA. In relation to the reporting of prognostic factors, less than 50% of studies included prognostic factors for DFC (47%), in-hospital mortality (40%), anastomotic leak (10%), perioperative mortality, enteroatmospheric fistula, ventral hernia and abscesses (7%). If there were a greater number of studies reporting prognostic factors in regard to these outcomes their results would provide vital information in the hope of improving the outcomes of patients being managed with an OA.

Finally, there are a multitude of factors affecting the overall outcome of OA patients, from the reliability of intensive care unit support, quality of surgical intervention, severity of underlying disease, and patient characteristics. This article focuses primarily on prognostic factors associated with DFC, mortality, and intra-abdominal complications.

CONCLUSIONS

The OA has attracted a great deal of interest over the last two decades. Persistent intra-abdominal infection, delays in obtaining DFC and poor preoperative state (acute renal failure or unconsciousness) appear to have the greatest effect on morbidity and mortality in OA patients. Prognostic factors identified in this systematic review allow for an enormous amount of potential for early intervention in the hope of reducing patient mortality and complications. Careful selection and management of OA patients will also aid in avoiding prolonged treatment and facilitate better patient outcomes. Future research should focus on the development of a prognostic model in regard to outcomes for DFC, perioperative and in-hospital mortality and the development of intra-abdominal complications.

AUTHORSHIP

Study concept and design was carried out in consultation by A.C. with his supervisors K.H., R.G., and A.D.C.A.C. was involved in all aspects of the project. S.J. was involved in independently reviewing articles, as well as performing data extraction and methodological assessment of the included studies. All authors gave their approval for the article before submission.

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DISCLOSURE

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