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Impact of ABO blood group on mortality in trauma patients: A systematic review☆

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ABSTRACT

Background: Haemorrhage is a significant cause of death in trauma patients. There is evidence that individuals with blood group O have higher rates of non-traumatic haemorrhage. It has been suggested that blood group O may be associated with higher mortality in trauma, however existing evidence is limited and conflicting.
Objective: A systematic review was conducted to evaluate the impact of ABO blood group on mortality in trauma patients.
Methods: MEDLINE via OVID, the Cochrane library and grey literature were searched to identify studies investigating the effect of ABO blood group on mortality of trauma patients admitted to hospital. PRISMA guidelines were followed throughout, study quality was assessed using CASP checklists and certainty of evidence was evaluated using GRADE. Meta-analysis was precluded by significant study heterogeneity.
Results: 180 relevant records were screened and seven studies met inclusion criteria, representing 12,240 patients. Two studies found that there was a higher mortality in blood group O compared to other ABO groups. Included studies had substantial variability in methods and population. Study quality was variable with certainty of evidence rated as very low.
Conclusions: There is insufficient evidence to definitively establish an association between mortality and ABO group in trauma patients. In an age of increasingly individualised care, there is a need to determine the existence and cause for any association through further studies across multiple settings, trauma mechanisms and populations.

1. Introduction

Trauma is a leading cause of death worldwide, accounting for approximately 10 % of all deaths [1]. Exsanguination is responsible for the majority of deaths in the first 24 h following traumatic injury [2,3]. Extensive research efforts surrounding haemorrhage have reduced the number of these potentially preventable deaths, in areas such as transfusion, damage control resuscitation, and improving our knowledge of trauma-induced coagulopathy, however the influence of ABO blood group on trauma-associated mortality remains undetermined.

The ABO blood group system classifies blood according to the antigen type expressed on erythrocytes, platelets, vascular endothelium and other tissues [4]. Most widely known for its relevance to transfusion and transplant medicine, previous studies have also established an association between haemostasis and ABO group in various settings. Blood group O is an independent risk factor for haemorrhage in postpartum haemorrhage [5], upper gastrointestinal haemorrhage [6], bleeding in cardiac [7] and orthopaedic surgery [8], and general haemorrhage [9]. Furthermore, ABO classification has been demonstrated to profoundly influence risk of thromboembolic disease [9–12].

A proposed mechanism for this association is that individuals with blood group O have up to 35 % less von Willebrand factor (vWF) [13–15]. vWF is a glycoprotein that is fundamental to haemostasis, playing an essential role in mediating subendothelial platelet adhesion

Abbreviations: vWF, von Willebrand Factor; ISS, Injury Severity Score; AIS, Abbreviated Injury Scale; CASP, Critical Appraisal Skills Programme; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ICU, Intensive Care Unit; TBI, Traumatic Brain Injury; TICH, Traumatic Intracranial Haemorrhage; RTS, Revised Trauma Score.

☆ Review registration: PROSPERO CRD42022375781

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and promoting aggregation of activated platelets [14,16–19]. Additionally, vWF is a carrier for factor VIII and protects it from premature proteolytic degradation [20].

Despite this theoretical mechanism, previous studies focussing on trauma cohorts have not reached a consensus, and the importance of blood group on mortality in trauma remains controversial. The objective of this systematic review is to evaluate the available evidence on the impact of ABO blood group on mortality in adult trauma patients.

2. Methods

This systematic review followed PRISMA guidelines [21] and was prospectively registered with PROSPERO (CRD: 42022375781) on 8th December 2022.

2.1. Objectives

Primary objective: To determine whether there is sufficient evidence to support an impact of ABO blood group on mortality in trauma patients.

2.2. Search strategy

A systematic search for online literature was conducted using MEDLINE via OVID and the Cochrane Library from database inception to April 2023. Searches involved a combination of keywords and MeSH headings. Following completion of independent searches by two authors, results were compared and disagreements resolved through discussion. Searches took place on 21st February 2023, with a re-run of searches on 2nd April 2023 prior to final analysis. The search strategy for MEDLINE via OVID is presented in Table 1.

Unpublished studies and grey literature were sought from manual searching of relevant conference proceedings, organisational websites (including the British Society for Haematology [22], the British Orthopaedic Association Standards for Trauma [23], the Trauma Audit and Research Network [24]), thesis papers, bibliographies of relevant texts and other such resources. There were no limits on language or year of publication. Use of translation services was sought to further assess non-English language studies deemed to be potentially relevant. A comparative search via EMBASE did not yield any additional papers.

2.3. Study selection and eligibility criteria

Studies must meet the following criteria to be included:
Population – adult trauma patients admitted to hospital.
Exposure – type O blood group.
Comparison – other ABO blood groups.
Outcomes – mortality (all-cause).
Study design – cohort, case-control and cross-sectional studies (given the nature of the exposure group, randomised controlled trials are not possible).

Table 1
MEDLINE via OVID search strategy.

	Search term
1	Blood group*
2	Blood type*
3	ABO blood group [MeSH]
4	1 or 2 or 3
5	Trauma*
6	Wounds and injuries [MeSH]
7	5 or 6
8	Mortality
9	Death*
10	Mortality [MeSH]
11	8 or 9 or 10
12	4 and 7 and 11

Following a pilot search, it was evident that 'trauma' and 'mortality' were not consistently defined or characterised in available studies. Most studies used Injury Severity Score (ISS), or Abbreviated Injury Scale (AIS) for particular body regions, however they were not all directly comparable in their inclusion criteria. Mortality was variably defined as in-hospital, 30-day or not otherwise stated. Therefore, the authors have not added further specification to the population criteria regarding the definition of trauma or mortality, to avoid exclusion of potentially relevant studies. Additionally, major burns represent a unique trauma population. Wide variability in underlying traumatic mechanism, associated injuries, and pathogenesis (including likelihood of haemorrhage and coagulopathy) could inherently alter outcome and therefore preclude comparison. Thus, burns-only studies were excluded.

2.4. Data extraction

Each study identified was examined using pre-defined inclusion and exclusion criteria outlined above. Studies were excluded based on examination of the title and abstract alone if they clearly did not meet the defined criteria. If unclear, full text was sought for further examination.

Data were recorded onto a standardised data extraction form which was pilot-tested prior to usage. Generic study information was extracted: first author name, year of publication, source, source type, study title, country of origin, and study design (Appendix A). Specific data were also extracted: sample size, p-value, and data grouped by ABO blood groups of participant gender, mean age, ethnicity, blood group proportions, and mortality (*n* and odds ratio data). Data were extracted by two independent authors in a blinded process, with discrepancies resolved through discussion. When insufficient information was included in the publication, the named author was contacted for further details.

2.5. Risk of bias and quality assessment

Two authors independently assessed quality of evidence both by study and by outcome. Quality of individual studies was assessed using the relevant Critical Appraisal Skills Programme (CASP) checklists commonly used for cohort or case-control studies [25,26]. CASP is designed to stimulate discussion around whether study results are valid, including risk of bias (Section A), what the results are (Section B) and if results help locally (Section C) [25]. Risk of bias and quality of evidence for outcome of mortality was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool [27].

3. Results

The MEDLINE via OVID search yielded 123 records of relevance, with a further 57 from grey literature. The Cochrane Library did not yield any relevant records. Of the 180 studies screened, nine were sought for retrieval. One study was excluded as it focused on critically ill patients of which trauma was a small subset, and mortality data by ABO group for trauma subsets were not provided [28]. Miller et al. [29] measured mortality as a secondary outcome. This was a secondary analysis of the PROPRR trial data [2] where all patients received transfusions; with a median of eight red blood cell units received per patient, this population will inherently have different mortality risks and altered blood phenotypes and was therefore excluded. The selection and extraction process is further detailed in a PRISMA chart (Fig. 1).

3.1. Study characteristics

All studies were retrospective cohort studies except Reilly et al. [30] which was a prospective cohort study. Of the seven included studies, two originated from Japan (involving a similar author group), four from the United States, and one from Germany. Five studies [30–34] included general, undifferentiated trauma patients, one study [35] focussed on

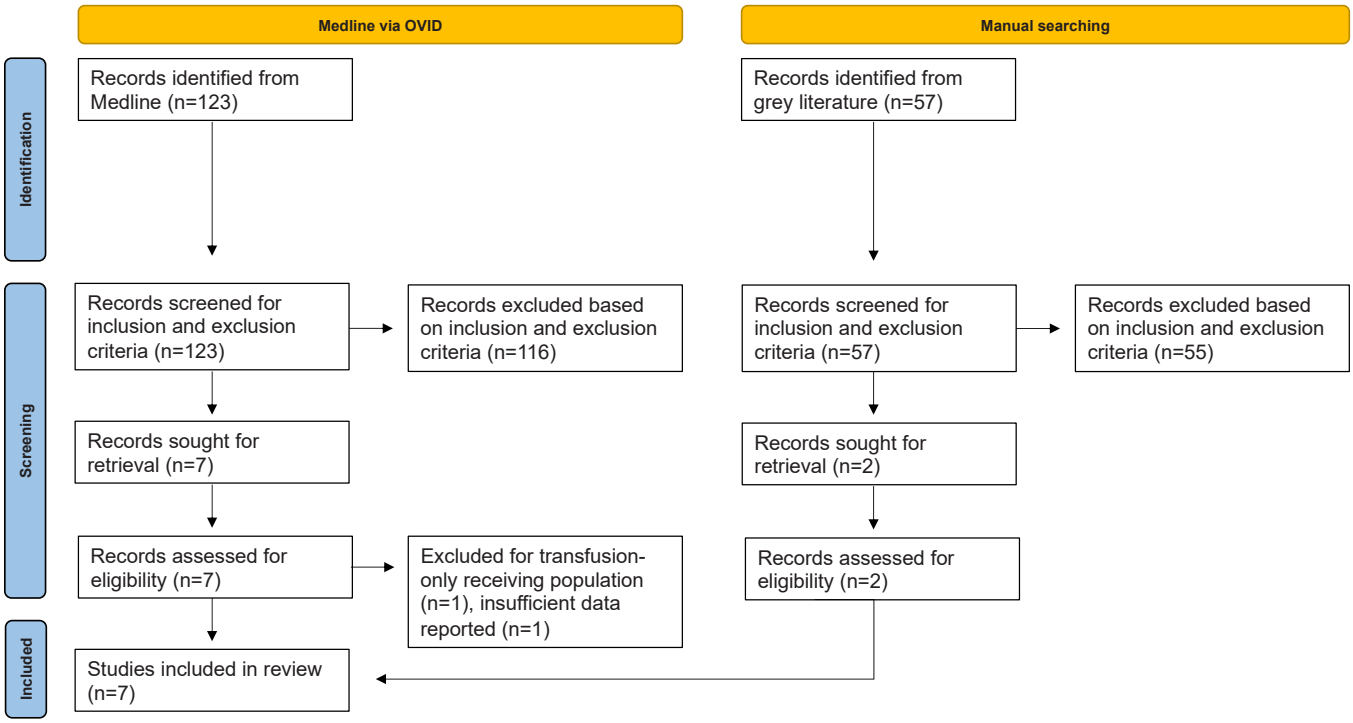

Fig. 1. PRISMA flow chart detailing the identification, screening and included records from MEDLINE via OVID and manual searching of the grey literature.

several abdominal trauma defined as AIS scores of three or more for abdomen and two or less for other body regions (see Table 2), and one study [36] included isolated blunt traumatic intracranial haemorrhage. There was significant heterogeneity between study criteria based on ISS, requirement for intensive care unit (ICU) admission, and inclusion of traumatic brain injury (TBI) patients.

Generic study information and demographics of included studies are presented in Table 2. All included studies had comparable mean age and gender proportions. Ethnicity was only reported in four studies [30,33,34,36] and therefore is not presented. All studies except Sauder et al. had a mean ISS > 15, which is generally used to define major trauma [37]. Wide variations in sample size were seen between 497 and 3913 patients. The substantial differences in populations and trauma mechanisms were not sufficiently homogenous to allow for appropriate meta-analysis and therefore a narrative synthesis is presented.

3.2. Study results

Two of the seven included studies reported that blood group O was significantly associated with higher mortality (Table 3) [31–35]. Sauder et al.[34] found that blood group O had higher mortality only in their small cohort sustaining penetrating injuries. This finding has not been seen elsewhere although other studies undertook limited comparison of blunt versus penetrating mechanism. Takayama et al. in 2018[31] found significantly higher deaths due to exsanguination in blood group O, despite the relatively high incidence of traumatic brain injuries (TBI) in this cohort. Hamsen et al. found that blood group O was the only group with a higher than predicted mortality and all other blood groups had an odds ratio for mortality below one, however, this was not statistically significant after multivariate logistic regression[32].

Table 2
Generic study information and demographics of included studies. Blood type proportions, mean age and male gender are listed as O:A:B:AB groups for ease of presentation. ISS and percentages of blood type proportions, male gender and mean age are rounded to the nearest whole number.

Authors	Year	Country of origin	Population	Sample size	Blood type proportions (%)	Mean age (years)	Male gender (%)	Mean ISS for all groups
Reilly et al.	2015	USA	Single centre, ISS > 15, ICU admission, excluded isolated TBI	497	45:33:16:6	32:39:39:47	78:72:68:78	22
Takayama et al.	2018	Japan	Two centres, ISS > 15	901	32:32:23:14	57:56:58:54	78:79:74:79	19
Hamsen et al.	2019	Germany	Three centres, ISS ≥ *9, ICU admission*	1281	37:44:13:6	50*	69:68:76:70	21
Griffin et al.	2020	USA	Single centre, ISS > 15	3913	48:35:13:3	45:45:44:45	71:70:74:76	25
Sauder et al.	2021	USA	Single centre, 'moderate and high trauma activations'	3779	47:38:12:3	47:49:46:48	65:60:61:69	10
Takayama et al.	2021	Japan	Twelve centres, severe abdominal trauma (AIS ≥3)	920	31:38:20:11	48:42:51:42	66:72:72:68	18
Tutunjian et al.	2021	USA	Single centre, isolated blunt TICH	949	46:39:13:4	O = 65 non-O = 64**	O = 55 non-O = 61**	17

TBI = traumatic brain injury, TICH = traumatic intracranial haemorrhage, ISS = injury severity score
* Hamsen et al. presented age as mean across the population and did not break this down by ABO subgroup.
** Tutunjian et al. presented age and gender as mean for O and non-O groups.

Table 3
Mortality results for included studies.

Authors	Year	Mortality by ABO group (%)	p-value	Adjusted odds ratio (OR) (95 % CI)	p-value
Reilly et al.	2015	7: 13: 6: 4	0.11	Data not presented	Data not presented
Takayama et al.	2018	28: 11: 14: 9	< 0.001	2.86 (1.84-4.46)	<0.001
Hamsen et al.	2019	13: 10: 10: 7	No significant difference	Data for group O not presented	No significant difference
Griffin et al.	2020	14: 13: 14: 10	No significant difference	1.09 (0.79 – 1.20)*	No significant difference
Sauder et al.	2021	4: 4: 3: 6	No significant difference	For penetrating injury only: 2.4 (1.1-5.4)	0.017
Takayama et al.	2021	22: 14: 15: 5	< 0.001	1.48 (1.25-2.26)	0.012
Tutunjian et al.	2021	O = 3 non-O = 4**	0.17	Data not presented	Data not presented

Mortality by ABO group is reported in the O:A:B:AB format.
* Griffin et al. [33] reported OR with blood group O as the reference compared to the other ABO groups, while the remaining studies reported the impact of group O on outcome – Griffin et al.'s OR have been inversed here for ease of comparison with other studies.
** Tutunjian et al. presented their mortality data in the O versus non-O blood group format.

3.3. Risk of bias and quality assessment

All seven studies addressed a clearly focussed issue with acceptable cohort recruitment. An important omission in three studies was data collection on patient ethnicity, which is relevant to multiple blood group phenotypes [38] and may itself affect trauma outcomes [39]. Sauder et al. were contacted to clarify their definition of 'highest and moderate level trauma activations' but a response was not received. A summary of this quality assessment can be found in Table 4 with a more detailed assessment in Appendix B.

Risk of bias and quality assessment of study outcomes assessed using GRADE are summarised in an evidence profile (Table 5), using guidance for GRADE assessment for narrative summaries[40]. Significant heterogeneity between study design and inclusion criteria introduced selection bias that limits outcome reliability. Additionally, there was failure to adequately control confounding variables, such as ethnicity. There was further downgrading due to inconsistent study results, with unexplained heterogeneity in odds ratios. Funnel plots were not used to assess for publication bias as there were fewer than 10 studies (as per GRADE recommendations). However, both the positive studies included had relatively small cohorts, and are published by the same author group, which could introduce bias. Overall, this resulted in a certainty rating of the evidence as very low.

4. Discussion

This systematic review summarises the findings from seven cohort studies that investigated the relationship between ABO blood group and mortality following traumatic injury. Quality assessment of the studies revealed mixed results, with substantial differences between the studies that limit generalisability of findings. Certainty of evidence was very low due to inconsistency and risk of bias in observational studies. Fundamental differences between study populations prevented sufficient comparability to allow appropriate meta-analysis.

We have demonstrated that the impact of ABO group on mortality is equivocal; two studies found a significant difference [31,35], one found a significant difference in a limited cohort [34], one found a trend towards mortality [32], and the remaining studies found no difference [30,33,36]. The reasons for these differences in outcome are unclear and likely multifactorial; they may be attributable to variations in study population (particularly inclusion of TBI patients within some studies), influence of ABO group on haemorrhage, ethnicity, or study setting.

In the interval between conducting and publishing this study, a review that was not indexed with PROSPERO has been published by Lubkin et al. [41] Their review included a number of additional studies which we have excluded. For example, Kander et al. [28] only included a trauma subset without any mortality data for this population, Miller et al. [29] featured a trauma cohort where transfusion was a prerequisite and mortality was a secondary outcome within a secondary analysis (the primary study did not evaluate ABO group), and Uzoigwe et al. [42] was exclusively hip fracture patients, and thus it is not possible to fairly compare these groups. Additionally, Lubkin et al. [41] undertook a meta-analysis despite significant heterogeneity within the included studies.

Takayama et al. [31] found that group O was an independent risk factor for mortality among trauma patients when controlling for age and injury severity, equivalent in impact to an increase in ISS of 12 or age of 26 years. One criticism of this study was the high proportion of brain

Table 4
Simplified quality appraisal results using the CASP checklist [25] for cohort studies. + = yes, - = no, ? = can't tell.

Question		Reilly	Takayama	Hamsen	Griffin	Sauder	Takayama	Tutunjian
		2015	2018	2019	2020	2021	2021	2021
Section A	1	+	+	+	+	+	+	+
	2	+	+	+	+	+	+	?
	3	+	+	+	+	+	+	+
	4	+	+	+	+	+	+	+
	5a	+	-	-	+	+	-	+
	5b	+	-	-	+	-	-	-
	6a	+	+	+	+	?	+	+
	6b	+	+	+	+	?	+	+
Section B	7	No significant difference	Higher mortality in O	No significant difference	No significant difference	Higher mortality in O only in penetrating injury cohort.	Higher mortality in O	No significant difference
	8	n/a	-	n/a	+	-	+	n/a
	9	+	+	+	+	?	+	-
Section C	10	?	?	+	+	?	?	-
	11	?	-	?	?	?	-	?
	12	-	Identifying higher risk patients	Trend only, authors question relevance to clinical practice	-	Further investigation into penetrating injuries, possible future guidelines	Identifying higher risk patients	-

Table 5
Summary of evidence profile for GRADE assessment of certainty of evidence for the outcome of mortality.

Certainty Assessment							Certainty
Number of participants (studies)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	
12,240 (7)	Observational	Serious	Serious	Not serious	Not serious	Suspected	Very low ⊕OOO

injured patients (median AIS head = 4) and thus potentially limited applicability to other settings.

The inclusion of TBI patients across studies was variable; the significance of ABO group on TBI outcomes remains undetermined. In a non-trauma setting, group O has previously been demonstrated to influence expansion of spontaneous intracranial haemorrhage [43] and incidence of midline shift [44]. This finding was not reproduced in Tutunjian et al.'s [36] cohort of traumatic intracranial haemorrhage patients. However, their cohort may not be representative of that seen within a trauma centre setting, as overall mortality was very low (3–4 %), over 80 % of patients had a fall mechanism, no patients had midline shift, and patients requiring surgical intervention following initial CT were excluded.

Correspondingly, Griffin et al. [33] also included a relatively large proportion of brain-injured patients but did not identify a difference in mortality by blood group, even when adjusting to the regression technique used by Takayama et al. [31]. One noteworthy difference in the Griffin et al. cohort is the considerably lower incidence of exsanguination compared with Takayama et al. (2018).

The hypothesis that ABO group is most important in the context of bleeding (and thus may not contribute as significantly to outcome in other pathologies, such as TBI) is also pertinent to other studies. Takayama et al. [35] subsequently demonstrated an association between group O and mortality in patients with isolated abdominal injuries, and therefore a likely haemorrhagic pathology [45]. However, it is noteworthy that compared to other blood groups, the group O cohort had a significantly lower Revised Trauma Score (RTS) and higher median AIS for abdomen and pelvis, which may have influenced the observed difference in mortality. Additionally, group O patients had a greater incidence of surgical intervention (21.5 % vs 14.6 %) compared to non-O patients, which may reflect their inherently greater injuries or need for haemorrhage control.

Sauder et al. [34] found a significant difference in mortality of blood group O patients only in their penetrating injury cohort. All other included studies had a similar percentage of penetrating and blunt trauma but did not compare outcomes in these populations. Sauder et al.'s population was the only study to have a mean ISS < 15, which may explain why a difference was not seen in all injury cohorts. It has previously been demonstrated that exsanguination is more likely following penetrating injury [46] with 51.7 % of penetrating injury patients compared with 12.5 % of blunt injury patients dying of exsanguination in a prospective multicentre study [47]. Therefore, we may speculate that the observed differences in results are attributable to the possibility that ABO groups, with their respective differences in vWF levels, most greatly influence mortality when the mechanism is likely to produce haemorrhage, as in Takayama et al.'s 2021 study [35].

Debot et al. [48] further substantiated this relationship between blood group and haemorrhage in their study of hypotensive trauma patients, establishing a vulnerability in group O patients to developing hyperfibrinolysis, which translated to an increase in requirement for massive transfusion. Takayama et al. [35] also found a significant increase in transfusion volume in their group O population; but no difference in early transfusions in their cohort of predominantly head injured patients, again suggesting that haemorrhagic pathology may be significant in the observed mortality difference.

Another possible explanation for the contradictory results observed is the contribution of study setting, ethnicity, and fundamental differences in trauma system infrastructure. For example, Griffin et al. [33] speculated that the coordinated regional trauma network at their study centre may have contributed to the lack of mortality difference observed. A number of potential confounders could exist between trauma networks, for example, access to prehospital life-saving interventions such as definitive airway management, blood transfusion and haemorrhage control via resuscitative thoracotomy [49,50]. There may also be differences in hospital care, for example thromboelastography was not consistently used in studies to guide transfusion and coagulopathy management.

The prevalence of each ABO group is variable worldwide [51–53]; for example in the United Kingdom 48 % of individuals are group O [54] versus approximately 31 % in the included Japanese studies [31–35]. Given the established differences in vWF levels in each blood group [14], and thus a potential susceptibility to impaired haemostasis [17], it is feasible that large differences in the prevalence of each blood group may contribute to observed differences in outcomes. Furthermore, ethnicity is known to influence haemostasis: for example, African Americans have higher levels of factor VIII, vWF, and activation markers of coagulation [55–57]. Of the included studies, only Griffin et al. [33] and Reilly et al. [30] made any adjustment for ethnicity, respectively identifying that group B patients were significantly more likely to be black and conducting a priori analyses for race. Given the highly homogenous Japanese population [58], any contribution of ethnicity to ABO-associated mortality could explain the contradictory results between the Japanese and other studies.

This review has several limitations. The inclusion of retrospective, non-randomised, and single centre cohort studies could introduce selection and confounding bias. Several studies performed adjustments for confounders such as age and ethnicity, however, these adjustments were not consistently implemented, and other confounders remain including non-standardised trauma care, transfusion thresholds, and injury mechanisms. The two papers with a positive association between ABO type and mortality were both from the same author group with overlapping timeframes, which could potentially introduce bias. However, these papers featured different populations: one with exclusively abdominally injured patients, while the other had an AIS for abdomen of zero. Given that ABO blood type is an exposure group and not an intervention, it is not possible to include higher levels of evidence such as randomised controlled trials. The review may be limited by challenges with defining mortality and trauma, which were not further specified to avoid excluding relevant studies. The decision not to restrict our definitions resulted in substantial differences in included studies, potentially limiting comparability and conclusions drawn. As discussed, appropriate meta-analysis was prevented by wide heterogeneity in trauma mechanism (with subsequent likelihood of exsanguination), ethnicity, and trauma setting. A significant proportion of included patients were predominantly head-injured or otherwise injured without suggestion of uncontrolled haemorrhage; therefore, within this cohort it is not possible to draw firm conclusions whether haemorrhage is a significant characteristic in any association with ABO.

5. Conclusions

The relationship between ABO blood group and trauma-associated mortality has a plausible mechanism, but current evidence is contradictory and insufficient. Existing studies demonstrate substantial

variability in methods, populations, and results. There is a need to determine the cause for any association, if one exists, as ABO group may influence mortality predominantly in the context of haemorrhagic pathology. In an age of increasingly personalised medicine, establishing this could facilitate a therapeutic intervention pathway for at-risk individuals, including stratification of thresholds for blood transfusion. Further studies across multiple healthcare settings, trauma mechanisms and populations are needed to definitively establish if ABO blood group affects mortality in trauma.

Ethics approval

Ethical approval did not apply to this study as it did not involve any human participants or animals.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest

None.

Appendix A. Example of completed generic study data extraction form

Entry	First author	Year	Source	Source type	Study title
1	Christian	2022	Archives of Pathology & Lab Medicine	Journal	Outcomes of Cold-Stored, Low-Titer Group O Whole Blood Transfusions in Nontrauma Massive Transfusion Protocol Activations

Appendix B. Detailed quality assessment of studies using CASP

Question		Study						
		Reilly (2015)	Takayama (2018)	Hamsen (2019)	Griffin (2020)	Sauder (2021)	Takayama (2021)	Tutunjian (2021)
A	1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	2	Yes – ISS > 15 admitted to surgical ICU	Yes - ISS > 15, 2 centres	Yes – ISS ≥ 9 and required ICU admission	Yes - > 15, single centre	Yes - single centre, high and moderate level trauma activations	Yes – severe abdominal injury, 12 hospitals	Can't tell – excluded patients requiring surgery after initial CT
	3	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	4	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	5a	Yes – analyses a priori stratified by race	No - ethnicity not included	No – ethnicity not included	Yes – ethnicity included	Yes - ethnicity included	No – ethnicity not included	Yes – ethnicity included
	5b	Yes	No	No	Yes – also tested matched regression analysis to Takayama (2018)	No - confounders such as ethnicity not controlled for	No	No – significant differences in pre-existing conditions
	6a	Yes	Yes	Yes	Yes	Can't tell – unclear if 'initial hospitalisation' encompassed entire hospital admission	Yes	Yes
	6b	Yes	Yes	Yes	Yes	Yes	Yes	Yes
B	7	No significant difference in mortality	Higher in-hospital mortality of blood group O including from exsanguination	No significant difference in mortality overall, however greater than predicted mortality for blood group O	No significant difference in mortality	Can't tell - unclear definition of mortality and 'trauma activation' In penetrating injuries there was increased mortality in blood group O, in blunt injuries blood group AB had higher mortality compared with all other groups.	Higher in-hospital mortality of blood group O. Increased transfusion requirements	No significant difference in mortality
	8	Odds ratios and associated confidence intervals not presented	Wide confidence intervals	Odds ratios and associated confidence intervals not presented	Relatively precise compared with other studies	Wide confidence intervals	Relatively precise compared with other studies	Odds ratios and associated confidence intervals not presented
	9	Yes	Yes - in isolation, however incongruent with other studies	Yes	Yes	Can't tell – mean ISS is much lower than other studies, and difference in mortality only seen in subcohort of penetrating injuries	Yes – in isolation, however incongruent with other studies	No – very short length of stay and low mortality, exclusion of all TBI patients requiring initial surgical intervention, majority of patients were falls mechanism (i.e. limited road traffic collisions and

(continued on next page)

(*continued*)

Question		Study						
		Reilly (2015)	Takayama (2018)	Hamsen (2019)	Griffin (2020)	Sauder (2021)	Takayama (2021)	Tutunjian (2021)
								other important mechanisms).
C	10	Can't tell – one centre, required surgical ICU admission	Can't tell – unclear significance of Japanese homogeneity	Yes – three trauma centres	Yes – large sample size, U.S. trauma centre	Can't tell - single U.S. trauma centre, low ISS therefore potentially not representative of major trauma	Can't tell – unclear significance of Japanese homogeneity	No – as above. Also, zero patients had midline shift which is unrepresentative of major trauma TBI.
	11	Can't tell	No – reports significant difference only seen in other Takayama paper	Can't tell – similar population to Griffin, with only trend towards bleeding in blood group O patients	Can't tell - no association found, even when using Takayama (2018) regression analysis	Can't tell - penetrating injuries found to be significant for blood group O but this was not investigated by other studies	No – reports significant difference only seen in other Takayama paper	Can't tell – this is the only isolated TBI paper, others included TBI variably with inconsistent findings.
	12	No robust evidence to suggest change for practice	Authors suggested risk recognition / resource planning to improve blood group O outcomes	Trend towards bleeding but no robust evidence	No robust evidence to suggest change for practice, authors suggest role of geographical differences	Authors suggest development of guidelines for resuscitation for blood groups once relationship to mortality better understood	Authors suggest identifying higher risk patients for determining level of treatment required	No robust evidence to suggest change for practice

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