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Sublingual microcirculation assessment in the Emergency Department for civilian and military patients with traumatic haemorrhagic shock: a pilot study

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Key words

Microcirculation; trauma; haemorrhage; sublingual; shock

ABSTRACT

Objectives

Sublingual microcirculatory monitoring for traumatic haemorrhagic shock (THS) may predict clinical outcomes better than traditional blood pressure and cardiac output, but is not usually performed until the patient reaches the Intensive Care Unit (ICU), missing earlier data of potential importance. This pilot study assessed for the first time the feasibility and safety of sublingual video-microscopy for THS in the Emergency Department (ED), and whether it yields useable data for analysis.

Setting

A safety and feasibility assessment was undertaken as part of the prospective observational MICROSHOCK study; sublingual video-microscopy was performed at the UK-led Role 3 medical facility at Camp Bastion, Afghanistan, and in the ED in three UK Major Trauma Centres.

Participants

There were 15 casualties (2 military, 13 civilian) who presented with traumatic haemorraghic shock with a median ISS of 26. Median age was 41; the majority (n=12) were male. The most common injury mechanism was road traffic accident.

Primary and secondary outcome measures

Safety and feasibility were the primary outcomes, as measured by lack of adverse events or clinical interruptions, and successful acquisition and storage of data. The secondary outcome was the quality of acquired video clips according to validated criteria, in order to determine whether useful data could be obtained in this emergency context.

Results

Video-microscopy was successfully performed and stored for analysis for all patients, yielding 161 video clips. There were no adverse events or episodes where clinical management was affected or interrupted. There were 104 (64.6%) video clips from 14 patients of sufficient quality for analysis.

Conclusions

Early sublingual microcirculatory monitoring in the ED for patients with THS is safe and feasible, even in a deployed military setting, and yields videos of satisfactory quality in a high proportion of cases. Further investigations of early microcirculatory behaviour in this context is warranted.

Trial registration

ClinicaTrials.gov Identifier: NCT02111109

ARTICLE SUMMARY

- Sublingual video-microscopy is a technique that enables direct visualization of the microcirculation, and may provide useful information during the resuscitation of patients with traumatic haemorrhagic shock (THS).
- No studies have reported early sublingual video-microscopy in the Emergency Department (ED) for patients with THS (i.e. before arrival in the Intensive Care Unit)
- This pilot study tests for the first time the safety and feasibility of performing sublingual video-microscopy for patients with THS in the ED, and assesses the quality of the video clips that were acquired.
- Data from this pilot study may help to guide other investigations into early microcirculatory behaviour following traumatic haemorrhagic shock

Strengths and limitations of this study

Although limited by a low number of patients and heterogeneity of injury patterns, this pilot study is the first to demonstrate safety and feasibility of sublingual video-microscopy in the Emergency Department for injured patients, including in a military environment following combat trauma. Further investigations are required to demonstrate whether this technique provides clinical useful data at such an early time-point.

BACKGROUND

There has been considerable interest in the disruption of the microcirculatory endothelium and endothelial glycocalyx following traumatic haemorrhagic shock (THS)[1]. Dysfunctional sublingual microcirculation following THS has been reported to be a good predictor of subsequent organ failure when measured in patients admitted to the Intensive Care Unit (ICU)[2]. The ability to maintain microcirculatory perfusion during early THS has been shown to be associated with more rapid reversal of the shock state during resuscitation in a large animal experimental model[3]. There may be some circumstances where microcirculatory flow does not follow global haemodynamics and parameters such as cardiac output and blood pressure no longer act as reliable surrogate markers for perfusion[4]. In such circumstances microcirculatory monitoring may offer more reliable guidance for resuscitation by adding information about true end-organ perfusion. The implications of bedside point of care microcirculatory parameters have not yet been realized but may have far-reaching utility in both civilian and military contexts.

Although it seems intuitive that microcirculatory readings from earlier time points closer to point of injury—especially before the definitive cessation of bleeding—may offer diagnostic and prognostic value following major trauma, this has not yet been investigated. It is possible that researchers have not attempted sublingual video-microscopy for trauma patients in the Emergency Department (ED) because of the constraints imposed by clinical urgency and environmental uncertainty, lack of capacity to consent, multiple interventions, and rapid transfer of the patient. Such a scenario is also likely to be noisy and crowded, with limited space and time at the

bedside – conditions that may be even more hostile in the deployed military context. Conversely, the ICU offers a more 'placid' environment with a stationary patient, increased space and time, and more stable physiology, even when patients are critically unwell. However, by the time of ICU arrival, patients may have received multiple resuscitative interventions, with unknown impact on the predictive value of sublingual video microscopy. It is therefore important to establish the feasibility of microcirculatory monitoring within the ED as a basis for studies to determine its clinical utility.

We present for the first time the feasibility of obtaining sublingual video-microscopy video clips during the emergency presentation of patients with THS. We hypothesized that non-invasive microcirculatory imaging in this emergency context is safe, feasible, and provides data of sufficient quality for meaningful analysis.

METHODS

Study design and setting

A prospective observational pilot study was undertaken to assess whether sublingual video-microscopy to image the microcirculation was feasible and safe for both civilian and military patients with THS, and whether the captured video clips were of high enough quality for analysis. Both civilian Research Ethics Committee (REC Ref 14/YH/0078) and Ministry of Defence Research Ethics Committee (MODREC Ref PPE 281/12) approvals were granted before the start of the study.

Patient selection

Patients were enrolled into the MICROSHOCK study (ClinicalTrials.gov Identifier: NCT02111109)[5]. Patients were eligible for inclusion if they had sustained major trauma with a likelihood of haemorrhage, and had a serum lactate value greater than 2mmol/L. Patient were recruited as soon as possible after arrival at three UK Major Trauma Centres (Queen Elizabeth Hospital, Birmingham; Kings College Hospital and Royal London Hospital, London). This was either in the ED or Intensive Care Unit (ICU). The current study includes the first 13 civilian patients recruited in ED and a further 2 deployed soldiers enrolled in the ED at the Role 3 medical facility in Camp Bastion during the Afghanistan conflict.

Sublingual video-microscopy

Sublingual microcirculation was visualized in the civilian patients using incident dark field (IDF) video-microscopy (Cytocam, Braedius Medical B.V., Huizen, The Netherlands). Military patients were scanned using a sidestream dark field (SDF) device (MicroVision Medical, Amsterdam, The Netherlands). IDF is a newer technology with higher resolution and larger field of view, but produces comparable results[6]. The devices are positioned towards the sublingual mucosa and maneuvered until a clear image of the microcirculation is acquired. Video clips (preferably lasting at least 5 seconds each) are then recorded and stored for offline analysis. At least 3 (but preferably 5) individual video clips are required for data analysis according to consensus agreement[7], but this does not limit the number of videos that can be captured. In this study as many videos as possible were recorded to ensure a sufficient number of analysis quality. For SDF video images continuous

video was taken rather than short clips; this was later spliced into high quality segments (each lasting 5 seconds) for computer analysis.

Capacity and consent

Due to the nature of the injuries sustained and physiological status of patients, capacity to consent was absent. The REC-approved consent process for enrollment in the study was guided by the Mental Health Act, UK (2005) and is explained in more detail in the study protocol[5]. In short, the physician in charge of the care of the patient (Nominated Consultee) agreed on the participation of the patient. A close friend or relative could also be approached if appropriate to act as a Personal Consultee. Ultimately if the participant regained capacity they were asked for their permission to retain data already collected.

Data collection

Patient demographics (age, sex) and injury-related details (mechanism of injury, injury severity score (ISS)) were recorded. Physiological parameters from the pre-hospital evacuation and ED included lowest systolic blood pressure (SBP), lowest Glasgow Coma Score (GCS), and highest lactate (as a surrogate for perfusion). The number and type of blood products were recorded as a measure of haemorrhagic burden. Details regarding sublingual video-microscopy included timings of video capture, profession of user, mechanism of notification of user, number of video clips stored, total length of video capture, and type of consent were also noted.

Outcomes

The outcomes of interest were: (i) safety (absence of adverse events or interference

with clinical management); (ii) feasibility (successful acquisition and storage of video clips); and (iii) the attainment of videos of high enough quality for meaningful data analysis. Quality assessment was undertaken according to a standardized technique that grades 6 domains for each video (including illumination, duration, focus, content, stability, and pressure artifact)[8]. The assessor was blinded to clinical status of the patient. Each domain was graded as optimal (0 points), suboptimal but still useable (1 point), or unacceptable and unusable (10 points). If any video clip has a score of 10 in any domain then the video was deemed unusable.

RESULTS

Patient characteristics

There were 15 patients (13 civilians and 2 military) included in the study. The majority of patients (12/15, 80%) were male; the median age was 41 (IQR 30 – 55) years.

Injury burden and physiology

The most common injury mechanism was road traffic accident (n=7), followed by crush injury (n=2), fall (n=2), penetrating trauma (n=1), and struck by a train (n=1). One military patient had been injured in an improvised explosive device (IED) blast; the other had been crushed by an armored vehicle. The median ISS for all patients was 26 (23 – 34). The median lactate in ED was 4.6 (interquartile range (IQR) 2.8 – 7.9) mmol/L. Median SBP was 79 (IQR 68 – 105) mmHg, and median lowest GCS before intubation was 9 (IQR 5 – 12). Patients in this group received a median of 4 (IQR 1.5 – 6) units of RBCs, 2 (IQR 0 – 5) units of FFP, and 0 (IQR 0 – 0.5) units of platelets within the first 24 hours. The military patient injured by the IED received 32

units of RBCs, 31 units of FFP and 5 units of platelets.

Video-microscopy

The IDF device was used for 13 civilian patients, and the SDF device was used for the 2 military patients. Figure 1 illustrates a flow diagram of microcirculatory video acquisition. Video-microscopy was performed by a doctor for 12 patients and nurse for 3 patients. On all occasions these healthcare professionals were alerted to the arrival of the patient by phone call from the relevant ED. Video-microscopy was performed a median of 80 (IQR 58–138) minutes after arrival of the patient at the hospital. Enrollment was agreed by a Nominated Consultee on all occasions. Where a CT was performed as part of trauma management, this preceded sublingual video-microscopy in all instances.

Safety and feasibility

Video-microscopy was successfully performed and videos stored for analysis for all patients enrolled in ED. 161 video clips were stored for analysis, including 151 from civilian patients and 10 from military patients (the long continuous videos acquired for the military patients were spliced into 5 clips each). The median time at the bedside for video capture was 6 (IQR 5 – 8) minutes. There were no adverse events, and no incidents reported where clinical management was affected or patient care interrupted.

Quality assessment of videos

Of all videos retained for analysis, 104/161 (64.6%) were of suitable quality for computer analysis. These videos were acquired from 14 of the patients, with one

patient having no useable data. A median of 6 (IQR 5 – 10) video clips per patient were eligible for analysis, exceeding the 3 – 5 clips recommended by consensus guidance[7]. The median quality assessment score for useable videos was 2 (IQR 1 – 2).

DISCUSSION

The main finding from this study is that early sublingual microcirculatory monitoring in the Emergency Department is feasible and safe for patients with THS, and yields videos that can be used for analysis. Investigation of patients with THS can be performed using this technique without apprehension of interference in clinical management or detriment to the patient. Furthermore, if these data are deemed to be useful at the bedside to guide and direct resuscitation, then point of care microcirculatory monitoring may become an additional technique in the armory of the trauma clinician. Such non-invasive scanning modalities are commonplace during trauma resuscitation when they are considered to add valuable information, including focused assessment with sonography for trauma (FAST), and ultrasound to guide fluid therapy[9]. Associated training and ongoing validation would be essential components if this technique were to be used in clinical practice.

Obstacles and limitations

There are known obstacles in the acquisition of early microcirculatory data, which were confirmed in this feasibility study. Patients with THS are critically unwell, and their treatment is urgent and needs to progress uninterrupted. Transfers to radiology, ICU or operating theater cannot be paused for data acquisition without strong justification. Sublingual videomicroscopy has potential to overcome some of these

limitations because it is mobile and can follow the patient. We report that it takes a matter of minutes to undertake, and that there was a point in the patient pathway in all cases before patient transfer during which opportunistic videomicroscopy was suitable. In all occasions where cross-sectional imaging was undertaken, videomicroscopy was performed afterwards.

Although feasibility has been demonstrated, one patient had no videos clips of high enough quality for assessment. Time constraints and interference with video acquisition may increase the risk of such occurrences, and would require continued education, training, and maintenance of appropriate skills for data capture in less than ideal (and sometimes adverse) circumstances. User-dependency is a common feature of scanning modalities. Clinical judgment continues to be the optimal management strategy for these emergency scenarios with or without the additional data that microcirculatory monitoring might yield.

The majority of sublingual microcirculatory monitoring is conducted in the research domain, and early bedside point of care monitoring of the microcirculation for patients with THS has not been reported. Although limited by a small number of patients, the current study adds to the growing body of evidence that may justify and facilitate the transition of microcirculatory monitoring from research into clinical practice. Restoration of tissue perfusion by directing fluid and inotropic resuscitation towards microcirculatory targets appears to be a viable technique, but is yet to be tested. Some investigators have proposed that plasma may improve microcirculatory function due to its restorative properties[10]. Detection of microcirculatory dysfunction may have a role in guiding the choice or volume of fluids. Since acquisition of early microcirculatory data is feasible, it is timely to design and

implement appropriate studies to examine whether microcirculatory goal directed therapy is of benefit to patients.

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Contributorship statement

SDH conceived, designed and developed the MICROSHOCK study. DNN, MJM and TH contributed to study design modification and protocol amendments. Video acquisition for military patients was undertaken by MJM in Afghanistan. The remainder were performed by DNN and MJM (Birmingham), JM, IS and TH (Royal London), and SDH and CM (Kings College London). IMS implemented the military study in Birmingham. DNN wrote the manuscript, and all other authors contributed to the development, revision and final version.

Competing of interests

All authors declare that they have no conflicts of interests. Any opinions expressed in this work are the authors' own and do not necessarily represent those of the UK Defence Medical Services.

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Data sharing statement

No additional data available.

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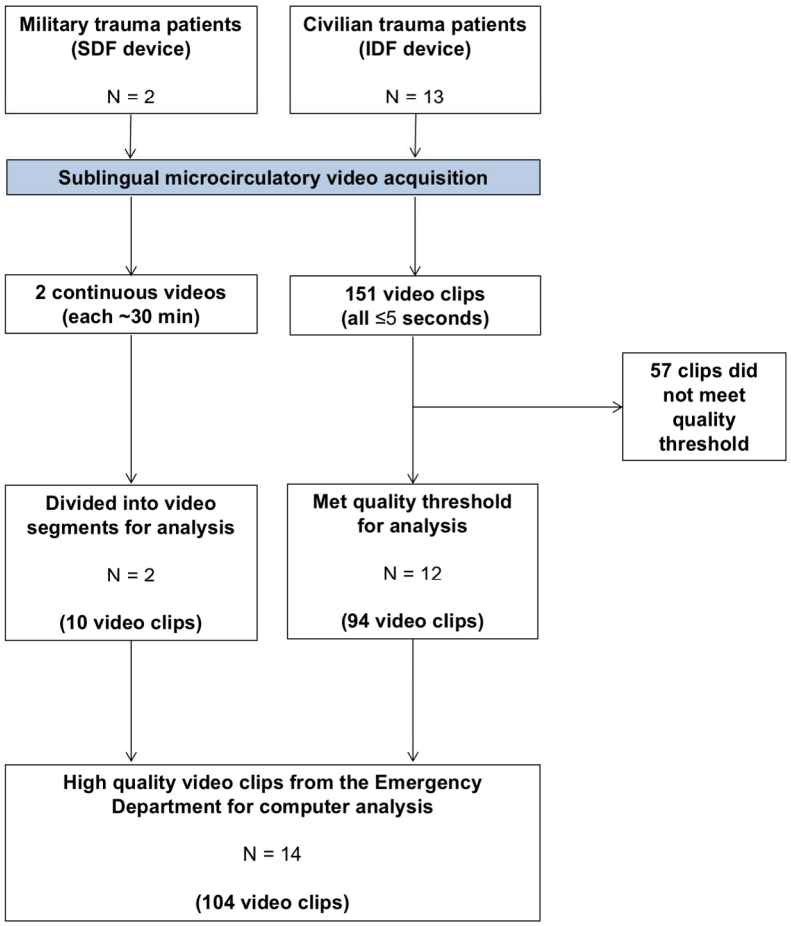
Figure legends

Figure 1. Flow diagram of microcirculatory video clip acquisition for computer analysis (N indicates the number of study participants at each stage)



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Key words

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ABSTRACT

Objectives

Sublingual microcirculatory monitoring for traumatic haemorrhagic shock (THS) may predict clinical outcomes better than traditional blood pressure and cardiac output, but is not usually performed until the patient reaches the Intensive Care Unit (ICU), missing earlier data of potential importance. This pilot study assessed for the first time the feasibility and safety of sublingual video-microscopy for THS in the Emergency Department (ED), and whether it yields useable data for analysis.

Setting

A safety and feasibility assessment was undertaken as part of the prospective observational MICROSHOCK study; sublingual video-microscopy was performed at the UK-led Role 3 medical facility at Camp Bastion, Afghanistan, and in the ED in three UK Major Trauma Centres.

Participants

There were 15 casualties (2 military, 13 civilian) who presented with traumatic haemorraghic shock with a median ISS of 26. Median age was 41; the majority (n=12) were male. The most common injury mechanism was road traffic accident.

Primary and secondary outcome measures

Safety and feasibility were the primary outcomes, as measured by lack of adverse events or clinical interruptions, and successful acquisition and storage of data. The secondary outcome was the quality of acquired video clips according to validated criteria, in order to determine whether useful data could be obtained in this emergency context.

Results

Video-microscopy was successfully performed and stored for analysis for all patients, yielding 161 video clips. There were no adverse events or episodes where clinical management was affected or interrupted. There were 104 (64.6%) video clips from 14 patients of sufficient quality for analysis.

Conclusions

Early sublingual microcirculatory monitoring in the ED for patients with THS is safe and feasible, even in a deployed military setting, and yields videos of satisfactory quality in a high proportion of cases. Further investigations of early microcirculatory behaviour in this context is warranted.

Trial registration

ClinicaTrials.gov Identifier: NCT02111109

Strengths and limitations of this study

- This study is the first to report sublingual video-microscopy in the Emergency Department (ED) or in a deployed military environment for patients with traumatic haemorrhagic shock (i.e. before arrival in the Intensive Care Unit).
- Although this study is prospective and multi-centred, generalizability may be limited by the low number of patients and their clinical heterogeneity.
- Only safety and feasibility were assessed during this pilot study, and are presented without further analysis of the microcirculatory parameters of recorded video clips.
- Data from this pilot study may help to guide other investigations towards the study of early microcirculatory behaviour following traumatic haemorrhagic shock.

BACKGROUND

There has been considerable interest in the disruption of the microcirculatory endothelium and endothelial glycocalyx following traumatic haemorrhagic shock (THS)[1]. Dysfunctional sublingual microcirculation following THS has been reported to be a good predictor of subsequent organ failure when measured in patients admitted to the Intensive Care Unit (ICU)[2]. The ability to maintain microcirculatory perfusion during early THS has been shown to be associated with more rapid reversal of the shock state during resuscitation in a large animal experimental model[3]. There may be some circumstances where microcirculatory flow does not follow global haemodynamics and parameters such as cardiac output and blood pressure no longer act as reliable surrogate markers for perfusion[4]. In such circumstances microcirculatory monitoring may offer more reliable guidance for resuscitation by adding information about true end-organ perfusion. The implications of bedside point-of-care microcirculatory parameters have not yet been realized but may have far-reaching utility in both civilian and military contexts.

Although it seems intuitive that microcirculatory readings from earlier time points closer to point of injury—especially before the definitive cessation of bleeding—may offer diagnostic and prognostic value following major trauma, this has not yet been investigated. Some investigators have performed sublingual microcirculatory assessment in the Emergency Department (ED) for patients with sepsis[5] and acute decompensated heart failure[6], but this has not yet been done for trauma patients. It is possible that researchers have not attempted sublingual video-microscopy for trauma patients in the ED because of the constraints imposed by clinical urgency

and environmental uncertainty, lack of capacity to consent, multiple interventions, and rapid transfer of the patient. Such a scenario is also likely to be noisy and crowded, with limited space and time at the bedside – conditions that may be even more hostile in the deployed military context. Conversely, the ICU offers a more 'placid' environment with a stationary patient, increased space and time, and more stable physiology, even when patients are critically unwell. However, by the time of ICU arrival, patients may have received multiple resuscitative interventions, with unknown impact on the predictive value of sublingual video microscopy. It is therefore important to establish the feasibility of microcirculatory monitoring within the ED as a basis for studies to determine its clinical utility.

We present for the first time the feasibility of obtaining sublingual video-microscopy video clips during the emergency presentation of patients with THS in the ED. We hypothesized that non-invasive microcirculatory imaging in this emergency context is safe, feasible, does not interfere with clinical management, and provides data of sufficient quality for meaningful analysis.

METHODS

Study design and setting

A prospective observational pilot study was undertaken to assess whether sublingual video-microscopy to image the microcirculation was feasible and safe for both civilian and military patients with THS, and whether the captured video clips were of high enough quality for analysis. Both civilian Research Ethics Committee (REC Ref

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Patient selection

Patients were enrolled into the MICROSHOCK study (ClinicalTrials.gov Identifier: NCT02111109)[7]. Patients were eligible for inclusion if there was evidence of haemorrhagic shock, and all of the following features: (i) injury mechanism consistent with blood loss; (ii) the patient is intubated and ventilated; (iii) serum lactate concentration >2 mmol/L; and (iv) the patient has received any blood products during initial resuscitation. Patient were recruited as soon as possible after arrival at three UK Major Trauma Centres (Queen Elizabeth Hospital, Birmingham; Kings College Hospital and Royal London Hospital, London). This was either in the ED or Intensive Care Unit (ICU). The current study includes the first 13 civilian patients recruited in ED and a further 2 deployed soldiers enrolled in the ED at the Role 3 medical facility in Camp Bastion during the Afghanistan conflict.

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Sublingual microcirculation was visualized in the civilian patients using incident dark field (IDF) video-microscopy (Cytocam, Braedius Medical B.V., Huizen, The Netherlands). Military patients were scanned using a sidestream dark field (SDF) device (MicroVision Medical, Amsterdam, The Netherlands). IDF is a newer technology with higher resolution and larger field of view, but produces comparable results[8]. The devices are positioned towards the sublingual mucosa and maneuvered until a clear image of the microcirculation is acquired. Video clips (preferably lasting at least 5 seconds each) are then recorded and stored for offline

analysis using dedicated computer software (Automated Vascular Analysis V.3.02, Microvision Medical, The Netherlands). At least 3 (but preferably 5) individual video clips are required for data analysis according to consensus agreement[9], but this does not limit the number of videos that can be captured. In this study as many videos as possible were recorded to ensure a sufficient number of analysis quality. For SDF video images continuous video was taken rather than short clips; this was later spliced into high quality segments (each lasting 5 seconds) for computer analysis.

Training

Sublingual video-microscopy was undertaken by dedicated research clinicians and research nurses who had been trained in the technique by an expert user and the study's Chief Investigator (S.D.H.) to a standard suitable for clinical research. Training was undertaken paying particular attention to standard quality assessment variables[10], including the optimization of stability, focus and illumination, as well as reducing pressure artefact and ensuring that the field of view contained microcirculatory vessels. The rationale and details of these quality domains have been described in detail elsewhere[11]. Since all patients in the MICROSHOCK study are intubated, users are trained to access the sublingual area with the endotracheal tube *in situ*.

Capacity and consent

Due to the nature of the injuries sustained and physiological status of patients, capacity to consent was absent. The REC-approved consent process for enrollment in the study was guided by the Mental Health Act, UK (2005) and is explained in

more detail in the study protocol[7]. In short, the physician in charge of the care of the patient (Nominated Consultee) agreed on the participation of the patient. A close friend or relative could also be approached if appropriate to act as a Personal Consultee. Ultimately if the participant regained capacity they were asked for their permission to retain data already collected.

Data collection

Patient demographics (age, sex) and injury-related details (mechanism of injury, injury severity score (ISS)) were recorded. Physiological parameters from the pre-hospital evacuation and ED included lowest systolic blood pressure (SBP), lowest Glasgow Coma Score (GCS), and highest lactate (as a surrogate for perfusion). The number and type of blood products were recorded as a measure of haemorrhagic burden. Details regarding sublingual video-microscopy included timings of video capture, profession of user, mechanism of notification of user, number of video clips stored, total length of video capture, and type of consent were also noted.

Outcomes

The outcomes of interest were: (i) safety (absence of adverse events or interference with clinical management); (ii) feasibility (successful acquisition and storage of video clips); and (iii) the attainment of videos of high enough quality for meaningful data analysis. Quality assessment was undertaken according to a standardized technique that grades 6 domains for each video (including illumination, duration, focus, content, stability, and pressure artifact)[10] by a single assessor (D.N.N) who was blinded to clinical status of the patient. Each domain was graded as optimal (0 points), suboptimal but still useable (1 point), or unacceptable and unusable (10 points). If

any video clip has a score of 10 in any domain then the video was deemed unusable.

Minimizing potential sources of bias

All patients that triggered a trauma team activation were screened for inclusion in the study, and a log was kept in order to ensure that risk of selection bias was minimised. The training of all video-microscopists was supervised and regularly assessed by the Chief Investigator to minimise the risk of inter-user heterogeneity. Quality assessment of videos was kept blinded to clinical status of the patient, study site, and video-microscopist, so that quality grading was as unbiased and consistent as possible.

RESULTS

Patient characteristics

There were 15 patients (13 civilians and 2 military) included in the study. The majority of patients (12/15, 80%) were male; the median age was 41 (IQR 30 – 55) years. All patients were unconscious and intubated at time of study enrollment, and recruited into the study with agreement by a Nominated Consultee. There were no cases of subsequent withdrawal of consent from the patient once they regained capacity.

Injury burden and physiology

The most common injury mechanism was road traffic accident (n=7), followed by

crush injury (n=2), fall (n=2), penetrating trauma (n=1), and struck by a train (n=1). One military patient had been injured in an improvised explosive device (IED) blast; the other had been crushed by an armored vehicle. The median ISS for all patients was 26 (23 – 34). The median lactate in ED was 4.6 (interquartile range (IQR) 2.8 – 7.9) mmol/L. Median SBP was 79 (IQR 68 – 105) mmHg, and median lowest GCS before intubation was 9 (IQR 5 – 12). Patients in this group received a median of 4 (IQR 1.5 – 6) units of RBCs, 2 (IQR 0 – 5) units of FFP, and 0 (IQR 0 – 0.5) units of platelets within the first 24 hours. The military patient injured by the IED received 32 units of RBCs, 31 units of FFP and 5 units of platelets.

Video-microscopy

The IDF device was used for 13 civilian patients, and the SDF device was used for the 2 military patients. Figure 1 illustrates a flow diagram of microcirculatory video acquisition. Video-microscopy was performed by a doctor for 12 patients and nurse for 3 patients. On all occasions these healthcare professionals were alerted to the arrival of the patient by phone call from the relevant ED. Video-microscopy was performed a median of 80 (IQR 58–138) minutes after arrival of the patient at the hospital. Where a CT was performed as part of trauma management, this preceded sublingual video-microscopy in all instances.

Safety and feasibility

Video-microscopy was successfully performed and videos stored for analysis for all patients enrolled in ED. 161 video clips were stored for analysis, including 151 from civilian patients and 10 from military patients (the long continuous videos acquired for the military patients were spliced into 5 clips each). The median time at the

bedside for video capture was 6 (IQR 5 – 8) minutes. There were no adverse events, and no incidents reported where clinical management was affected or patient care interrupted.

Quality assessment of videos

Of all videos retained for analysis, 104/161 (64.6%) were of suitable quality for computer analysis. These videos were acquired from 14 of the patients, with one patient having no useable data. A median of 6 (IQR 5 – 10) video clips per patient were eligible for analysis, exceeding the 3 – 5 clips recommended by consensus guidance[9]. The median quality assessment score for useable videos was 2 (IQR 1 – 2). Of the 57 video clips that were unusable, 18 failed quality assessment on more than one domain. The remaining 39 video clips that failed due to a single quality domain included content (n=14), pressure (n=13), stability (n=6), illumination (n=3), focus (n=2) and duration (n=1)

DISCUSSION

The main finding from this study is that early sublingual microcirculatory monitoring in the Emergency Department is feasible and safe for patients with THS, and yields videos that can be used for analysis. Investigation of patients with THS can be performed using this technique without apprehension of interference in clinical management or detriment to the patient. Such non-invasive scanning modalities are commonplace during trauma resuscitation when they are considered to add valuable information, including focused assessment with sonography for trauma (FAST), and ultrasound to guide fluid therapy[12]. Associated training and ongoing validation would be essential components if this technique were to be used in clinical practice.

Patients in this study had a considerable injury burden, with additional haemodynamic compromise according to their physiological and biochemical parameters. Sublingual microcirculatory monitoring was still feasible in this context within the very first hours of their arrival in hospital. Although the clinical utility of such readings is yet to be realized, it is possible that the availability of additional data relating to tissue perfusion may be of value in the resuscitation of such patients. Point-of-care microcirculatory monitoring is not currently used in clinical practice, but innovations to move this technique from research to the clinical domain have been proposed by our group[13] and others[14]. If point-of-care microcirculatory monitoring is deemed to be a useful resuscitation end point then it would be important to obtain readings before, during and after interventions so that changes might be recorded. The current study did not use such methodology, but further investigations into the utility of this technique are warranted.

Obstacles and limitations

There are known obstacles in the acquisition of early microcirculatory data, which were confirmed in this feasibility study. Patients with THS are critically unwell, and their treatment is urgent and needs to progress uninterrupted. Transfers to radiology, ICU or operating theater cannot be paused for data acquisition without strong justification. Sublingual videomicroscopy has potential to overcome some of these limitations because it is mobile and can follow the patient. We report that it takes a matter of minutes to undertake, and that there was a point in the patient pathway in all cases before patient transfer during which opportunistic videomicroscopy was suitable. In all occasions where cross-sectional imaging was undertaken,

videomicroscopy was performed afterwards. The study investigators did not wish to interfere with the preparation or transfer of patients who needed urgent imaging. If the technique is found to have clinical utility, then there may be some justification in obtaining even earlier readings, and incorporating the technique into the resuscitative pathway.

Although feasibility has been demonstrated, one patient had no videos clips of high enough quality for assessment. Time constraints and interference with video acquisition may increase the risk of such occurrences, and would require continued education, training, and maintenance of appropriate skills for data capture in less than ideal (and sometimes adverse) circumstances. User-dependency is a common feature of scanning modalities. Clinical judgment continues to be the optimal management strategy for these emergency scenarios with or without the additional data that microcirculatory monitoring might yield. There were only two military patients included in this study, and the authors acknowledge that firm conclusions cannot be made with these limited data. Further validation is required in such an environment.

The majority of sublingual microcirculatory monitoring is conducted in the research domain, and early bedside point of care monitoring of the microcirculation for patients with THS has not been reported. Although limited by a small number of patients, the current study adds to the growing body of evidence that may justify and facilitate the transition of microcirculatory monitoring from research into clinical practice. Restoration of tissue perfusion by directing fluid and inotropic resuscitation towards microcirculatory targets appears to be a viable technique, but is yet to be tested. Some investigators have proposed that plasma may improve microcirculatory

function due to its restorative properties[15]. Detection of microcirculatory dysfunction may have a role in guiding the choice or volume of fluids. Since acquisition of early microcirculatory data is feasible, it is timely to design and implement appropriate studies to examine whether microcirculatory goal directed therapy is of benefit to patients.

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Contributorship statement

SDH conceived, designed and developed the MICROSHOCK study. DNN, MJM and TH contributed to study design modification and protocol amendments. Video acquisition for military patients was undertaken by MJM in Afghanistan. The remainder were performed by DNN and MJM (Birmingham), JM, IS and TH (Royal London), and SDH and CM (Kings College London). IMS implemented the military study in Birmingham. DNN wrote the manuscript, and all other authors contributed to the development, revision and final version.

Competing of interests

All authors declare that they have no conflicts of interests. Any opinions expressed in this work are the authors' own and do not necessarily represent those of the UK Defence Medical Services.

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Data sharing statement

No additional data available.

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Figure legends

Figure 1. Flow diagram of microcirculatory video clip acquisition for computer analysis (N indicates the number of study participants at each stage)

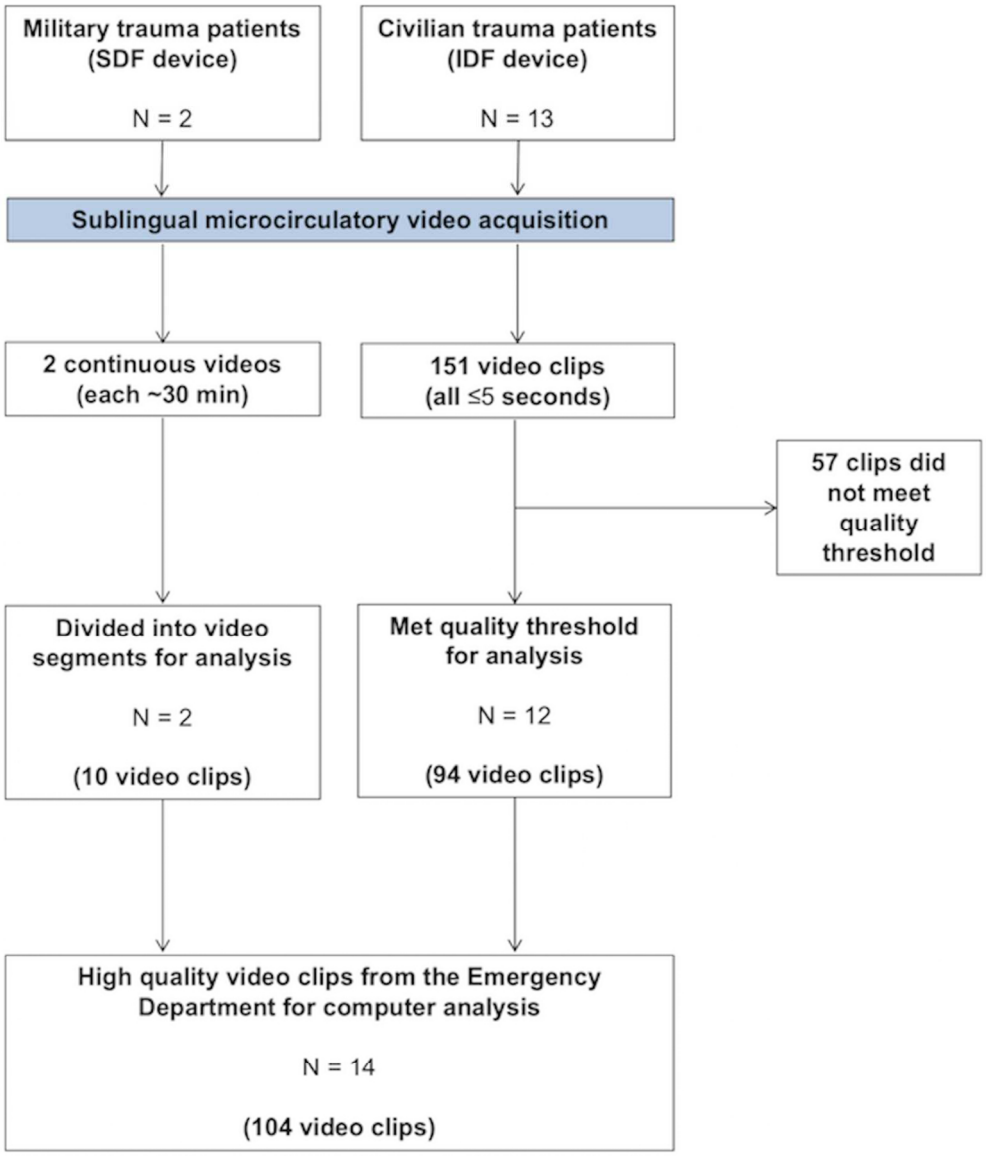

Figure 1. Flow diagram of microcirculatory video clip acquisition for computer analysis (N indicates the number of study participants at each stage)

105x123mm (300 x 300 DPI)

STROBE Statement: "**Safety and feasibility of sublingual microcirculation assessment in the Emergency Department for civilian and military patients with traumatic haemorrhagic shock: a prospective cohort study**"

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3, 4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6, 7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7,8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	None
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11

		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Report numbers of outcome events or summary measures over time	12,13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14,15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14,15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.