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ORIGINAL ARTICLE

Temporal patterns of neutrophil recruitment and microthrombus formation in fatal traumatic brain injury: a forensic histopathological study

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Abstract

Estimation of post-traumatic survival time represents a critical issue in forensic neuropathology. While secondary inflammatory and vascular responses after traumatic brain injury (TBI) are known to evolve over time, their intravascular compartmentalization and forensic applicability remain incompletely characterized. We conducted a retrospective histopathological and immunohistochemical study on brain tissue from 51 fatal TBI cases with documented post-traumatic survival times ranging from minutes to approximately two months, and 15 non-traumatic control cases. Neutrophil recruitment was assessed in meningeal and parenchymal cerebral vessels using CD15 immunohistochemistry. Parenchymal vessels were further stratified by caliber. The presence and characteristics of neutrophil-rich microthrombi were systematically evaluated and correlated with survival time. Minimal intravascular neutrophil presence was observed in cases of immediate death and in controls. Early post-traumatic survival was characterized by progressive neutrophil accumulation within meningeal vessels. With increasing survival time, neutrophil recruitment became more prominent in parenchymal vessels, particularly in larger-caliber vessels, and was associated with the appearance of neutrophil-rich microthrombi, which peaked during the subacute phase. In cases with prolonged survival, intravascular neutrophil counts and microthrombi progressively declined. Vascular-associated neutrophil recruitment and neutrophil-rich microthrombus formation follow consistent temporal patterns after fatal TBI. These findings support the forensic relevance of intravascular inflammatory changes as complementary histopathological markers for survival time estimation in fatal TBI.

Clinical trial number: not applicable.

Key Points

- Intravascular neutrophil recruitment after fatal traumatic brain injury shows a time-dependent distribution across meningeal and parenchymal vessels.
- Early post-traumatic phases are characterized by predominant neutrophil accumulation in meningeal vessels, followed by progressive involvement of parenchymal vessels.
- Neutrophil-rich microthrombi emerge during subacute survival intervals and peak between 3 and 8 days.
- These vascular inflammatory changes represent potential histopathological markers supporting survival time estimation in forensic neuropathology.

Keywords Traumatic brain injury · Forensic neuropathology · Survival time estimation · Neutrophils · Neuroinflammation · Microthrombi · Forensic immunohistochemistry.

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Introduction

Traumatic brain injury (TBI) represents one of the leading causes of death and disability worldwide and constitutes a frequent subject of medico-legal investigation, particularly in cases involving violent death, accidental trauma, or alleged malpractice [1–3]. From a forensic perspective, beyond the identification of traumatic lesions, a crucial issue is the estimation of post-traumatic survival time, which may corroborate or contradict investigative reconstructions and witness statements [2, 4].

Neuropathologically, TBI is classically divided into primary injury, occurring at the moment of impact, and secondary injury, which develops over time as a consequence of complex pathophysiological mechanisms, including ischemia, blood–brain barrier disruption, excitotoxicity, and inflammation [1, 2]. While primary lesions may be evident at autopsy, secondary injury processes are highly time-dependent and therefore represent a valuable source of chronological information in forensic practice [2, 4].

Among secondary mechanisms, neuroinflammation plays a central role in the evolution of traumatic brain damage. Experimental and human post-mortem studies have demonstrated that the inflammatory response of the central nervous system follows the typical sequence of innate immunity activation, involving endothelial activation, leukocyte recruitment, and progressive parenchymal involvement [3, 5]. In this context, the structural and functional alteration of the blood–brain barrier (BBB) facilitates the transmigration of circulating immune cells into the injured brain tissue [5, 6].

In forensic pathology, increasing attention has been devoted to the use of histological and immunohistochemical markers to improve the temporal assessment of traumatic lesions [1, 4]. Routine histology alone often lacks sufficient sensitivity to discriminate narrow survival intervals, especially in cases of short survival or subtle trauma [2]. Conversely, immunohistochemistry has proven capable of detecting early and progressive cellular responses, allowing a more refined estimation of injury timing with greater probative reliability [4, 5].

Several studies have investigated markers of neuronal damage, astrocytic activation, microglial response, and endothelial dysfunction to assist in the dating of TBI [4–6]. In particular, the evaluation of neuroinflammatory and endothelial activation markers has emerged as a promising approach, as inflammatory cell recruitment follows relatively predictable temporal patterns. Endothelial activation, leukocyte adhesion, and subsequent extravasation represent key events in secondary brain injury and may provide useful chronological indicators when interpreted in an integrated histopathological framework [5].

Despite these advances, significant limitations persist. Most proposed markers show considerable interindividual variability, are influenced by systemic and post-mortem factors, or lack sufficient specificity when used in isolation [2, 4, 6]. Moreover, the majority of studies have focused predominantly on parenchymal changes, whereas the intravascular inflammatory component, particularly in relation to vessel caliber and microthrombotic phenomena, remains comparatively underexplored in the forensic setting [4, 6].

Neutrophils are among the earliest immune cells recruited following traumatic injury and play a pivotal role in inflammation-associated vascular damage and thrombosis [3, 4]. Their temporal distribution within cerebral vessels, as well as their involvement in microthrombus formation, may therefore reflect the progression from acute to subacute post-traumatic phases. However, systematic post-mortem investigations correlating neutrophil dynamics within different vascular compartments with documented survival times are scarce [4].

The aim of the present study is to analyze neutrophil recruitment patterns within meningeal and parenchymal cerebral vessels, with particular attention to vessel caliber, and to correlate these findings with post-traumatic survival time in a series of fatal TBI cases. By integrating quantitative neutrophil assessment and the evaluation of neutrophil-rich microthrombi, this study seeks to contribute to the identification of reproducible histopathological features that may support survival time estimation in forensic practice. CD15 was selected as neutrophil marker due to its well-documented reliability and robustness in post-mortem tissue.

Materials and methods

Study design and case selection

This retrospective study included 51 cases of fatal TBI and 15 control cases that underwent medico-legal autopsies at the Institute of Legal Medicine of the University of Parma, Italy.

Inclusion criteria for TBI cases were: (i) documented TBI confirmed at medico-legal autopsy; (ii) availability of complete medico-legal documentation; (iii) availability of adequately preserved brain tissue suitable for histological and immunohistochemical analysis; (iv) reliable reconstruction of post-traumatic survival time based on clinical and investigative data. Post-traumatic survival time ranged from a few minutes to approximately two months, as determined from clinical and investigative records.

Exclusion criteria for TBI cases included: (i) advanced autolysis or inadequate tissue preservation; (ii) evidence of central nervous system infection or primary inflammatory brain disease; (iii) known systemic inflammatory or infectious conditions, when documented; (iv) incomplete clinical or investigative data preventing reliable survival time assessment.

Control cases consisted of subjects who died from non-traumatic and non-neurological causes, with no macroscopic or microscopic evidence of brain injury. Exclusion criteria for control cases included: (i) any evidence of TBI; (ii) central nervous system disease; (iii) known systemic inflammatory or infectious conditions; (iv) known prolonged agonal states potentially affecting vascular or inflammatory findings.

Autopsy procedure and tissue sampling

External examinations and full medico-legal autopsies were performed according to the guidelines of the European Council of Legal and Forensic Medicine (ECFLM) [7].

After removal, the brain was examined macroscopically. In TBI cases, tissue samples were systematically collected from contusional areas. In control cases, samples were obtained from brain regions without macroscopic or microscopic pathological alterations.

All specimens were fixed in 10% neutral-buffered formalin, routinely processed, and embedded in paraffin. Serial sections of 4 µm thickness were prepared for histological and immunohistochemical analyses.

Histological and immunohistochemical analysis

Routine histological evaluation was performed using hematoxylin and eosin (H&E) staining to assess tissue architecture, vascular alterations, inflammatory infiltrates, and secondary parenchymal damage.

Immunohistochemical staining was performed to identify neutrophils using antibodies against CD15 (clone Leu-M1, Agilent Dako). Positive and negative controls were included in each staining run to ensure antibody specificity and staining reproducibility.

Evaluation of neutrophil recruitment and microthrombi

Neutrophil recruitment was evaluated within meningeal and parenchymal vessels, with particular attention to differences related to vessel caliber. The distinction between small- and large-caliber parenchymal vessels was based on luminal diameter as an operational criterion. Parenchymal vessels with an internal diameter < 100 µm were categorized as small-caliber, while those ≥ 100 µm were considered large-caliber, in line with commonly used definitions in studies on microvascular structure and inflammation [8].

Microthrombi were defined as intravascular aggregates partially or completely occluding the lumen and containing platelet and/or granulocytic components. Neutrophil-rich microthrombi were operationally defined as intravascular aggregates partially or completely occluding the lumen and characterized by a predominance of granulocytic components. The presence, distribution, and morphological characteristics of microthrombi were systematically assessed. Microthrombi were classified according to their cellular composition into: (i) early platelet-rich microthrombi; (ii) mixed platelet–leukocyte thrombi; (iii) granulocyte-rich microthrombi, observed at later stages.

All findings were correlated with documented post-traumatic survival time.

Quantitative analysis

Quantification was performed by evaluating five high-power fields (HPFs) selected along a diagonal axis across the tissue section. This approach was adopted to ensure sampling across different areas of the section and to reduce the risk of focal overrepresentation of inflammatory changes in heterogeneous contusional tissue.

Fields were selected avoiding areas of tissue disruption, hemorrhagic artifacts, or processing-related damage, in order to include morphologically evaluable and representative regions.

In each field, neutrophils were counted within individual vessels, and results were expressed as the number of CD15-positive cells per vessel.

Results

Immediate death

In cases of immediate death, neutrophils were scarcely represented within meningeal vessels, with a mean value of approximately 4 neutrophils per vessel [Figure 1a]. Similarly, neutrophil recruitment within parenchymal vessels was minimal: most vessels showed a complete absence of neutrophils, while a limited number contained only 1–2 polymorphonuclear cells.

No neutrophil-rich microthrombi were observed.

At the parenchymal level, astrocytic activation was largely absent. In contrast, lesions attributable to primary traumatic injury, including micro- and macro-hemorrhages, vascular wall discontinuities, and tissue lacerations, were consistently present.

Survival from a few minutes to 2 h

During this early survival interval, an increase in neutrophils within meningeal vessels was evident, with a mean value of 16 neutrophils per vessel. Neutrophils appeared predominantly dispersed within the vascular lumen, without

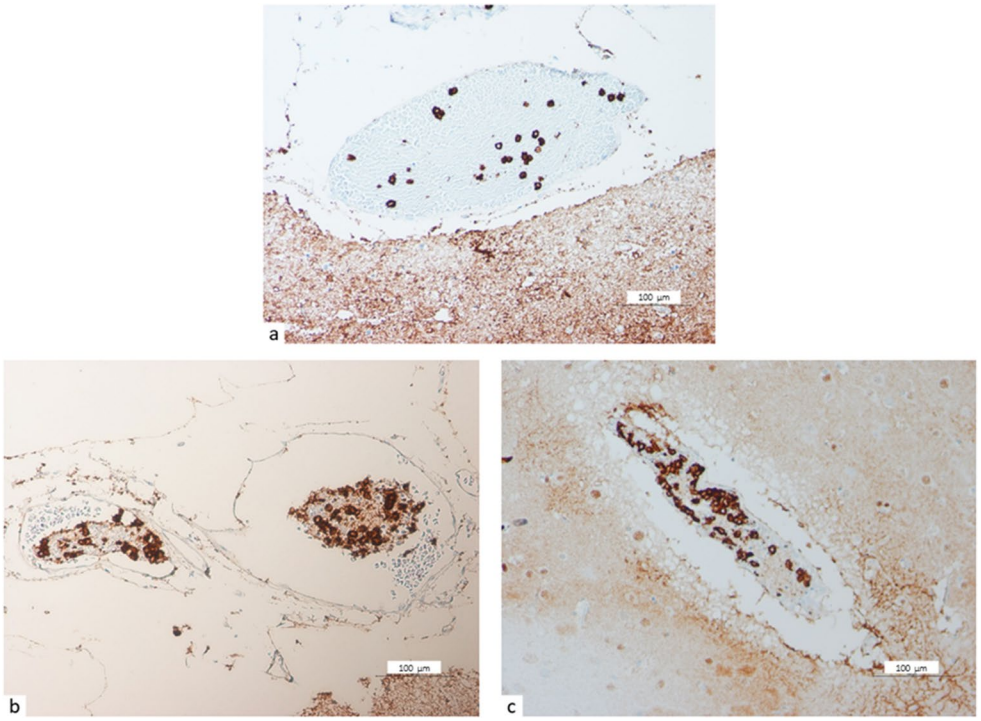

Fig. 1 (**a**–**c**). Temporal progression of intravascular neutrophil recruitment in meningeal vessels after TBI. CD15 immunohistochemistry; original magnification ×20. (**a**) Scattered CD15-positive neutrophils within a meningeal vessel in a TBI case with short survival (approximately 1 hour). (**b**) Increased intravascular CD15-positive neutrophil accumulation with early endothelial adhesion in a TBI case with a survival time of approximately 4 hours. (**c**) Marked intravascular accumulation of CD15-positive neutrophils with evident endothelial adhesion in a TBI case with a survival time of approximately 5 hours

evidence of adhesion to the endothelial surface. A mild increase was also observed in parenchymal vessels, with a mean value of 1.72 neutrophils per vessel.

No neutrophil-rich microthrombi were identified.

At the parenchymal level, early astrocytic activation was present, predominantly in perivascular regions. In addition, rounded cells morphologically consistent with glial elements were detectable within the parenchyma.

Survival from 2 to 5 h

Cases with survival times between 2 and 5 h demonstrated a marked increase in neutrophil recruitment within meningeal vessels, representing the first evident peak of inflammatory cell accumulation in this compartment [Fig. 1b and c]. A mean value of 33 neutrophils per vessel was recorded. In several vessels, neutrophils exhibited early adhesion to the endothelial lining. Parenchymal vessels also showed increased neutrophil counts, with a mean value of 2.17 neutrophils per vessel.

No microthrombi were detected.

At the parenchymal level, astrocytic activation and marked vascular congestion were consistently present.

Survival from 5 to 24 h

In this interval, neutrophil counts within meningeal vessels remained elevated, with a mean value of 26 neutrophils per vessel. Neutrophils displayed a clearly inflammatory distribution, preferentially localizing along the vessel periphery and extending into the perivascular tissue. In contrast, neutrophil recruitment within parenchymal vessels increased, with a mean value of 3.59 neutrophils per vessel.

Partially occluded vessels and early neutrophil-rich microthrombi were identified, predominantly involving small-caliber vessels. Parenchymal astrocytic activation and significant vascular congestion persisted throughout this interval.

Survival from 24 to 48 h

Between 24 and 48 h, neutrophil numbers within meningeal vessels remained significantly elevated, with a mean value of 31 neutrophils per vessel. A further increase in neutrophil recruitment was evident within parenchymal vessels, reaching a mean value of 4.46 neutrophils per vessel. In larger-caliber parenchymal vessels, substantially higher neutrophil counts were observed, with a mean value of 9.07 neutrophils per vessel.

Partially occluded vessels were frequently present, with a mean of 8 microthrombi per histological section.

Survival from 3 to 8 days

In cases with survival times between 3 and 8 days, a clear reduction in neutrophil counts within meningeal vessels was evident, with a mean value of 9.5 neutrophils per vessel. Neutrophil numbers within parenchymal vessels also declined, reaching a mean value of 3.7 neutrophils per vessel.

The number of neutrophil-rich microthrombi increased markedly [Fig. 2a, b, c and d], reaching its peak in the case with 8 days of survival, with a mean value of 44.5 microthrombi per section.

Parenchymal cellularity remained elevated and was associated with persistent astrocytic activation.

Survival longer than 8 days

In the two cases with survival times exceeding 8 days, neutrophil counts within meningeal vessels were low, with a mean value of 4.0 neutrophils per vessel, comparable to those observed in cases of immediate death and in control subjects. Similarly, parenchymal vessels showed limited neutrophil recruitment, with a mean value of 1.8 neutrophils per vessel.

The number of microthrombi was markedly reduced, with only 2 microthrombi identified in the case surviving approximately 2 months.

In this latter case, parenchymal neutrophils exhibited a reparative distribution, localizing at the periphery of hemorrhagic lesions showing features of organized clot formation.

Control cases

Control cases showed minimal and non-significant neutrophil presence in both meningeal and parenchymal vessels, with mean values of 2.86 and 1.29 neutrophils per vessel, respectively [Fig. 3a and 3b].

No parenchymal lesions, hemorrhages, or astrocytic activation were present. Overall cellularity was not increased, and microthrombi were absent.

Quantitative trends in neutrophil recruitment and neutrophil-rich microthrombus formation across survival groups are summarized in Table 1; Figs. 4 and 5 Given the descriptive nature of the analysis and the uneven distribution of cases across survival intervals, particularly in longer survival groups, the observed findings should be interpreted as indicative temporal trends rather than statistically validated patterns.

Discussion

Clinical and experimental studies consistently demonstrate a rapid recruitment of neutrophils to the injured brain, with accumulation occurring predominantly within the perivascular and microvascular compartments during the early post-traumatic phase [9, 10]. Neutrophil infiltration has been correlated with BBB disruption and worsening neurological outcome. Early neutrophil accumulation predominantly involves meningeal vessels, consistent with an earlier and more permissive inflammatory vascular response compared with parenchymal vessels, where neutrophil recruitment becomes more evident at later time points [3, 9].

A major mechanism by which neutrophils exacerbate post-traumatic damage is the formation of neutrophil extracellular traps (NETs). NETs, composed of decondensed

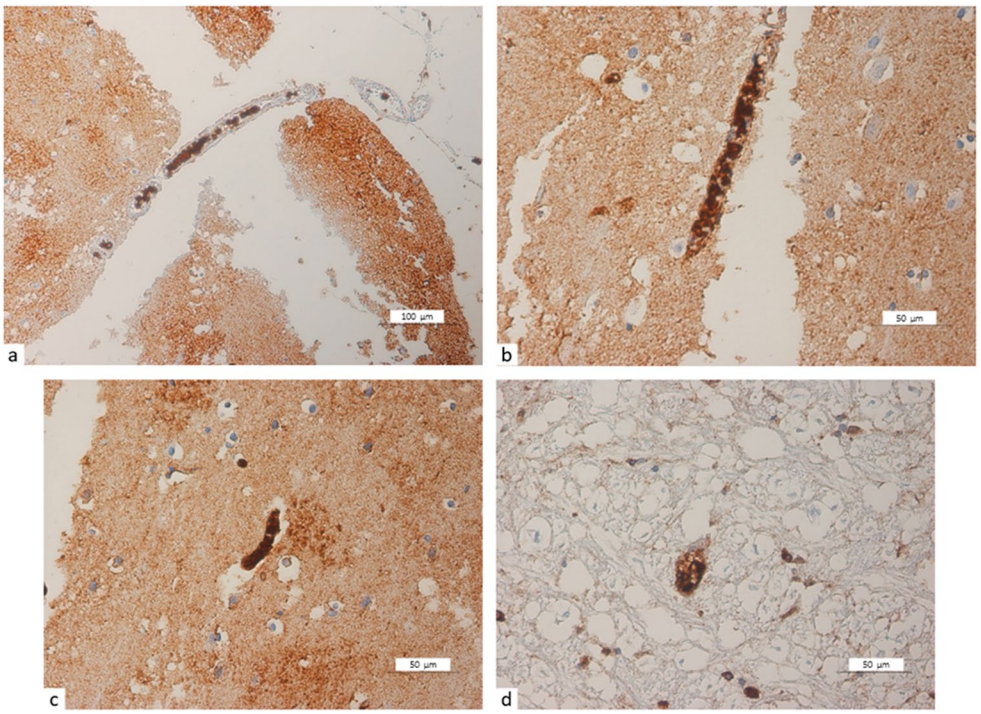

Fig. 2 Neutrophil-rich microthrombi in parenchymal cerebral vessels during the subacute phase after TBI. CD15 immunohistochemistry. (**a**) Neutrophil-rich microthrombus within a parenchymal cerebral vessel in a TBI case with a survival time of approximately 4 days. Original magnification x20. (**b**) (**c**) (**d**) High-power views showing neutrophil-rich microthrombi causing partial luminal obstruction in parenchymal cerebral vessels in TBI cases with subacute survival (4 days). Original magnification x40.

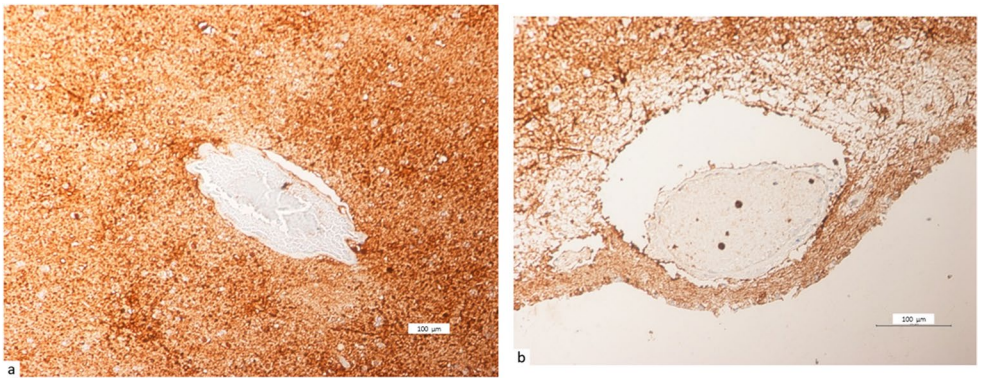

Fig. 3 Control cases showing absence of significant intravascular neutrophil recruitment. CD15 immunohistochemistry; original magnification ×20. (**a**) Parenchymal cerebral vessel from a control case showing absence of CD15-positive neutrophils. (**b**) Meningeal vessels from a control case showing absence of significant neutrophil accumulation.

Table 1 Mean neutrophil counts in meningeal and parenchymal vessels and mean number of microthrombi according to post-traumatic survival time. Parenchymal vessels were further stratified by caliber into large and small vessels. Values are expressed as mean counts per vessel or per histological section

Survival group	Meningeal vessels (mean neutrophils / vessel)	Parenchymal vessels (mean neutrophils / vessel)	Large parenchymal vessels (mean neutrophils / vessel)	Small parenchymal vessels (mean neutrophils / vessel)	Mean number of microthrombi
Immediate death	4.00	1.10	3.55	1.38	0.00
Few minutes – 2 h	16.00	1.72	2.06	1.54	0.00
2–5 h	33.00	2.17	4.13	1.96	0.00
5–24 h	26.00	3.59	10.48	2.60	6.00
24–48 h	31.00	4.46	9.07	3.48	8.00
3–8 days	9.50	3.70	8.42	2.80	44.50
>8 days	4.00	1.80	2.30	1.50	2.00
Controls	2.86	1.29	2.00	1.31	0.00

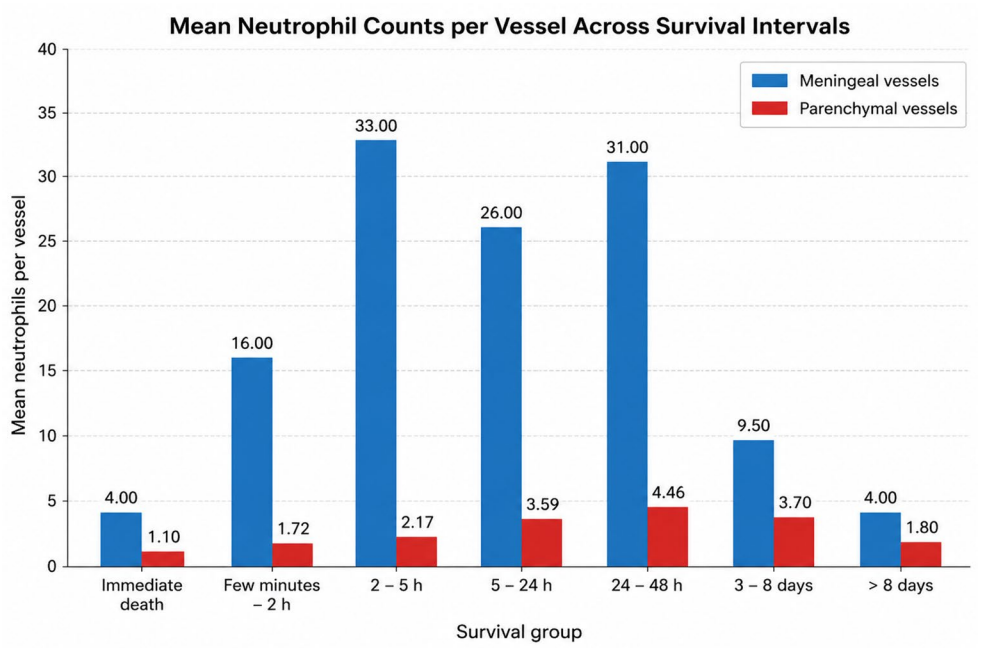

Fig. 4 Mean neutrophil counts per vessel in meningeal and parenchymal vessels across post-traumatic survival intervals. Blue bars represent meningeal vessels, while red bars represent parenchymal vessels

chromatin decorated with histones and granular proteins, have been shown to accumulate in contused brain tissue and circulation following TBI, where they promote endothelial injury, amplify neuroinflammation, and impair microvascular perfusion [11–13]. NET-associated components have been implicated in the activation of endothelial inflammatory pathways, loss of tight junction integrity, and increased vascular permeability [14, 15]. NETs also provide a scaffold for platelet adhesion and fibrin deposition, promote microthrombus formation, and contribute to microcirculatory

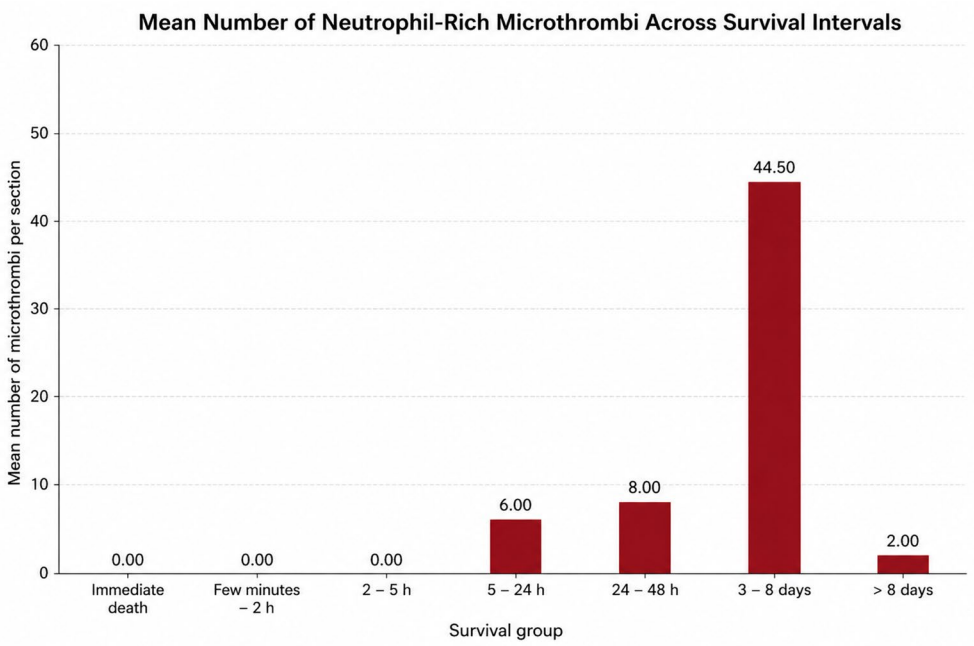

Fig. 5 Mean number of neutrophil-rich microthrombi per histological section across post-traumatic survival intervals.

failure [16, 17]. Inhibition of NET formation attenuates microvascular thrombosis, reduces cerebral edema, and improves neurological outcomes [18, 19]. Although NETs represent a plausible mechanistic link between inflammation and microthrombosis, they were not directly assessed in the present study. Therefore, their role should be considered hypothetical and requires further investigation.

In line with these experimental and clinical observations, the results of the present human post-mortem study document an earlier and more rapid accumulation of neutrophils within meningeal vessels, detectable already within minutes after TBI. In contrast, significant neutrophil recruitment within parenchymal vessels becomes evident only after several hours of post-traumatic survival. Similarly, the appearance of neutrophil-rich microthrombi represents a later event, requiring a minimum post-traumatic survival interval to become histopathologically appreciable.

The vascular compartment appears to be a critical interface for these processes. Endothelial cells respond to neutrophil-derived mediators by upregulating adhesion molecules, releasing damage-associated molecular patterns, and undergoing inflammatory forms of cell death [20, 21]. This bidirectional crosstalk further facilitates neutrophil adhesion, transendothelial migration, and NET deposition within and around cerebral vessels, reinforcing the concept of a neurovascular unit-centered pathology in TBI.

In this context, previous human post-mortem evidence further supports the temporal relevance of vascular inflammatory activation after TBI. Neri et al. (2018) documented a progressive increase in astrocytic activation, microglial response, and perivascular macrophage accumulation in cases with longer survival times, highlighting the close relationship between inflammation, edema formation, and hypoxic signaling [22]. Dressler et al. (2007) argued that apoptotic neuronal and glial changes appear within defined temporal windows following TBI, with caspase-3 activation and TUNEL positivity becoming detectable within hours after injury and persisting for days to weeks depending on survival time [23].

Recent forensic studies have further explored the temporal evolution of inflammatory responses across different anatomical compartments. In particular, Benevento et al. (2025) investigated the dura mater and highlighted its potential utility for survival time determination, also employing digital pathology approaches [24].

While their study focused on meningeal tissues and quantitative digital analysis, the present work specifically addresses intravascular inflammatory dynamics within brain tissue. Our vascular-centered approach provides direct insight into neurovascular interactions and microcirculatory alterations occurring after trauma.

Both studies support the concept that compartment-specific inflammatory responses exhibit time-dependent trends after TBI. In this context, the analysis of intravascular inflammatory changes within the brain parenchyma represents a complementary perspective to meningeal and digitally quantified approaches. Future integration of digital pathology techniques with vascular-centered histopathological analysis may further improve reproducibility and enhance the forensic applicability of these findings.

The findings of the present study are consistent with and extend this framework, suggesting that neutrophil infiltration

and microthrombotic phenomena follow distinct temporal trends across different post-traumatic survival intervals.

Our results indicate that, during the very early post-traumatic phase, neutrophil accumulation is predominantly confined to meningeal vessels, where neutrophils are observed within the vascular lumen in the absence of overt endothelial adhesion or transmigration. This pattern likely reflects the greater immune accessibility and earlier inflammatory responsiveness of meningeal vessels compared with parenchymal microvessels.

With increasing post-traumatic survival, neutrophil recruitment progressively involves parenchymal vessels, initially affecting larger-caliber vessels and subsequently extending to smaller-caliber microvessels. This progression may reflect the gradual amplification of endothelial activation and BBB dysfunction within the injured brain, allowing sustained leukocyte adhesion and intravascular accumulation. The preferential involvement of larger parenchymal vessels during intermediate survival intervals suggests that hemodynamic factors and endothelial surface properties may influence the spatial distribution of intravascular neutrophils.

Importantly, neutrophil-rich microthrombi do not appear as an immediate consequence of trauma but emerge during later post-traumatic phases, particularly in cases with survival extending beyond several hours. This temporal dissociation supports the concept that microthrombus formation represents a downstream event of sustained endothelial activation and neutrophil–endothelial interaction, rather than a primary mechanical consequence of injury. Once established, microthrombi may persist even as intravascular neutrophil counts begin to decline, reflecting ongoing microvascular dysfunction rather than active leukocyte recruitment alone.

Control cases showed no significant intravascular neutrophil accumulation or microthrombus formation, supporting the specificity of the observed vascular inflammatory changes to TBI.

These findings support a model in which early vascular neutrophil accumulation, progressive parenchymal vascular involvement, and subsequent microthrombus formation represent sequential stages of a shared neurovascular inflammatory response after TBI. The consistency of these patterns across defined survival intervals suggests that intravascular inflammatory changes may retain chronological information of forensic relevance.

Similar time-dependent dynamics have been recently observed in other biological systems in TBI, including mast cell activation and hypoxia-related pathways (CD117 and HIF-1α) [25]. The convergence of these independent markers further supports the biological plausibility of temporally stratified neurovascular responses after TBI.

In the forensic setting, the interpretation of TBI has increasingly relied on biochemical and molecular biomarkers measured in biological fluids to support diagnosis and postmortem investigations [26–28]. While valuable, these markers provide indirect and global information and are influenced by multiple confounding factors.

Against this background, the vascular compartment represents a particularly informative target for post-mortem investigation. Intravascular inflammatory changes, including neutrophil accumulation, can be reliably detected in post-mortem tissues and reflect pathological processes evolving before death [29]. The present findings suggest that the evaluation of intravascular neutrophils and neutrophil-rich microthrombi may offer a useful complementary approach to fluid-based biomarkers, supporting survival time estimation in fatal TBI within an integrated post-mortem forensic framework.

Limitations

A major limitation lies in the sampling strategy. In TBI cases, tissue samples were collected from contusional areas, whereas control samples were obtained from non-injured regions. This may introduce selection bias, as lesion-centered tissue is inherently enriched in vascular and inflammatory alterations. Therefore, differences between TBI and control groups should be interpreted with caution and cannot be attributed exclusively to temporal dynamics.

No systematic sampling of non-contusional regions in TBI cases was performed. Although macroscopically uninjured brain tissue was occasionally available, these samples were not consistently collected nor systematically analyzed. Therefore, the present study was designed as a lesion-centered analysis. While this approach increases sensitivity to pathological processes, it represents a limitation in terms of internal comparability.

The retrospective design did not allow systematic control of potential confounding factors, including agonal duration, resuscitation procedures, systemic inflammatory or infectious conditions, and anticoagulant therapy, all of which may influence intravascular neutrophil counts and microthrombus formation.

The quantitative approach based on the evaluation of five HPFs selected along a diagonal does not fully eliminate selection bias and may be influenced by local variability within contusional areas. In addition, neutrophil counts were expressed per vessel without normalization for vessel size or tissue area, which may limit reproducibility and comparability across cases. Future studies employing standardized stereological approaches or digital image analysis may improve quantitative robustness.

Finally, the limited number of cases with prolonged survival (>8 days) represents a further constraint, and findings in this subgroup should be considered preliminary.

Conclusions

TBI is a dynamic process in which secondary inflammatory and vascular mechanisms evolve over time after the initial insult. Neutrophil activation and microvascular dysfunction represent key components of this progression and are closely linked to post-traumatic survival.

The present study demonstrates that vascular-associated neutrophil infiltration and microthrombotic changes show consistent temporal patterns in human post-mortem brain tissue. By preserving anatomical context, these features provide direct evidence of biologically active processes related to survival time.

In a forensic perspective, the histological assessment of vascular-centered inflammatory changes may complement existing morphological and biochemical approaches, offering additional support for the estimation of survival time in TBI.

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Declarations

Ethics The study was conducted in accordance with national and institutional ethical standards and with the principles of the Declaration of Helsinki. Ethical consent: not applicable.

Competing Interests The authors declare that they have no competing interests.

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