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Diagnostic Discrepancies in Stroke Diagnostics: An Autopsy-Based Literature Review

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Abstract

Background and aims: Despite major advances in stroke diagnosis, autopsy studies continue to demonstrate discrepancies between premortem clinical diagnoses and postmortem findings. Accurate determination of the cause of death is essential for the development of stroke care and treatment. This review focuses on the diagnostic value of autopsy in stroke-related deaths by examining the concordance between clinical diagnoses and neuropathological findings.

Methods: A systematic literature review was conducted in PubMed, Embase, and the Cochrane Library. Eligible studies from 1985 onwards reported original autopsy findings and compared them with premortem clinical stroke diagnoses. Study selection and data extraction were performed independently by two reviewers using Covidence. Extracted data included study characteristics, sample size, autopsy rates, and reported diagnostic discrepancies.

Results: Of the 301 identified studies, 10 studies were included, comprising 1424 patients who died following a clinical stroke diagnosis, of whom 1104 patients underwent autopsy. Core areas of diagnostic discrepancy include: (1) 4 studies about under-recognition of stroke and stroke mechanisms, (2) 4 studies about missed intracranial pathology, and (3) 4 studies about systemic complications overlooked clinically.

Conclusions: Autopsy remains a valuable tool for diagnostic clarification in stroke by identifying clinically unrecognized pathology and correcting misclassified causes of death, such as systemic complications, despite advances in neuroimaging and clinical assessment. Autopsy should be considered if the cause of death and stroke aetiology are not certain or is atypical.

Keywords: Cerebrovascular diseases, autopsy, postmortem examination, clinical diagnosis, cause of death, stroke, apoplexy, ischemic stroke, hemorrhagic stroke, diagnostic errors, misdiagnosis, sudden death, unexpected death, mortality.

Introduction

Cerebrovascular disease represents a major public health challenge worldwide. Stroke is the second leading cause of mortality and long-term disability globally. Although stroke-related mortality rates have declined in both high- and low-income countries, the absolute number of stroke cases, survivors, deaths, cost, and associated disability continues to increase, largely driven by population ageing and improved survival (Feigin et al., 2025)(Donkor, 2018) (Wang, et al., 2025).

The pathological manifestations of stroke vary considerably according to subtype, anatomical distribution, and etiology. Comprehensive post-mortem examination combining thorough histological and macroscopic analysis is therefore essential for elucidating the mechanisms of stroke and providing clinically relevant information to healthcare teams, coronial authorities, and bereaved families. Despite its diagnostic value, the frequency of autopsy has declined markedly in recent decades across Europe and the USA. In Sweden, clinical autopsy rates decreased from nearly 40% to below 5% over a fifty-year period (Eriksson et al., 2021), while in the Netherlands, rates fell from approximately 31% in 1977 to 8% in 2011 (Kuijpers et al., 2017). A broader European review reported autopsy rates of less than 10% in countries such as Norway, Denmark, and Switzerland, with higher rates—up to 30%—in Finland, Austria, and several Eastern European nations (Karwinski et al., 2014). A similar trend has been observed in the United States, where the proportion of deaths undergoing autopsy declined from approximately 19.3% in 1972 to 8.5% in 2007, representing a reduction of more than 50% over this period (Hoyert, 2011). This decline has substantially limited opportunities for clinicopathological correlation in contemporary stroke care.

A proportion of stroke-related pathologies remain undetected until post-mortem examination. Autopsy enables direct neuropathological assessment and identification of intracranial and systemic conditions not recognized premortem, including small infarctions, hemorrhagic transformation, and contributory systemic disease. Consequently, post-mortem examination remains essential for confirming clinical diagnoses and clarifying mechanisms of stroke-related death, although declining autopsy rates limit contemporary pathological knowledge. This literature review was conducted to elucidate the correlation between clinical and neuropathological diagnoses in patients with stroke and unexpected death.

Method

Research Strategy

Relevant search terms and potential synonyms related to stroke, mortality, and diagnostic accuracy were identified and the terms were combined using Boolean operators (“AND” and “OR”) to delimit and refine the research scope.

The main search terms included *stroke*, *apoplexy*, *ischemic stroke*, *sudden death*, *unexpected death*, *cause of death*, *mortality*, *diagnosis*, *misdiagnosis*, *diag**, and *diagnostic errors*. Truncation “*” were applied to include all relevant word variants sharing the same word stem.

The final search string applied across all databases was: *((Stroke OR apoplexy OR ischemic stroke OR hemorrhagic stroke) AND (Sudden death OR unexpected death OR cause of death OR mortality OR death)) AND ((misdiagnosis OR diagnostic errors OR discrepancies) AND (autopsy OR postmortem examination OR biopsy))*.

The search was restricted to studies published from 1985 onwards, reflecting the introduction of magnetic resonance imaging (MRI) into routine diagnostic stroke protocols, and limited to English-language publications. Eligible studies were original research articles reporting autopsy findings and their comparison with clinical stroke diagnoses.

Information Sources

A comprehensive literature search was conducted in the following databases: PubMed, Embase, and the Cochrane Library. The search was initially performed independently by each author and subsequently refined collaboratively. To ensure completeness, additional sources, such as relevant conference proceedings and reference lists of the included studies, were also screened to include literature not indexed in the primary databases. The final search date was March 12, 2026.

All retrieved papers were imported into Covidence (Veritas Health Innovation, Melbourne, Australia), which initially automatically identified and removed duplicate entries. Screening was performed in three stages: (1) title screening, (2) abstract screening, and (3) full-text review. Two reviewers independently assessed each record (both first authors: BZG and HC). Reasons for excluding the studies will be systematically documented and recorded. Furthermore, discrepancies were resolved through discussion and consensus among the

authors or by referral to a third member of the review team (last author: ASW). Results of the selection process will be depicted in a flow diagram (**Figure 1**).

Data Extraction and Quality Assessment

Data extraction was conducted by using a template created by the authors in Covidence. Extracted variables included title, author & publication year, study design & study setting, Mean age $\pm$ SD, sample size, number of autopsies performed, and results highlighting the diagnostic concordance between clinical and postmortem findings, as well as identified sources of discrepancy.

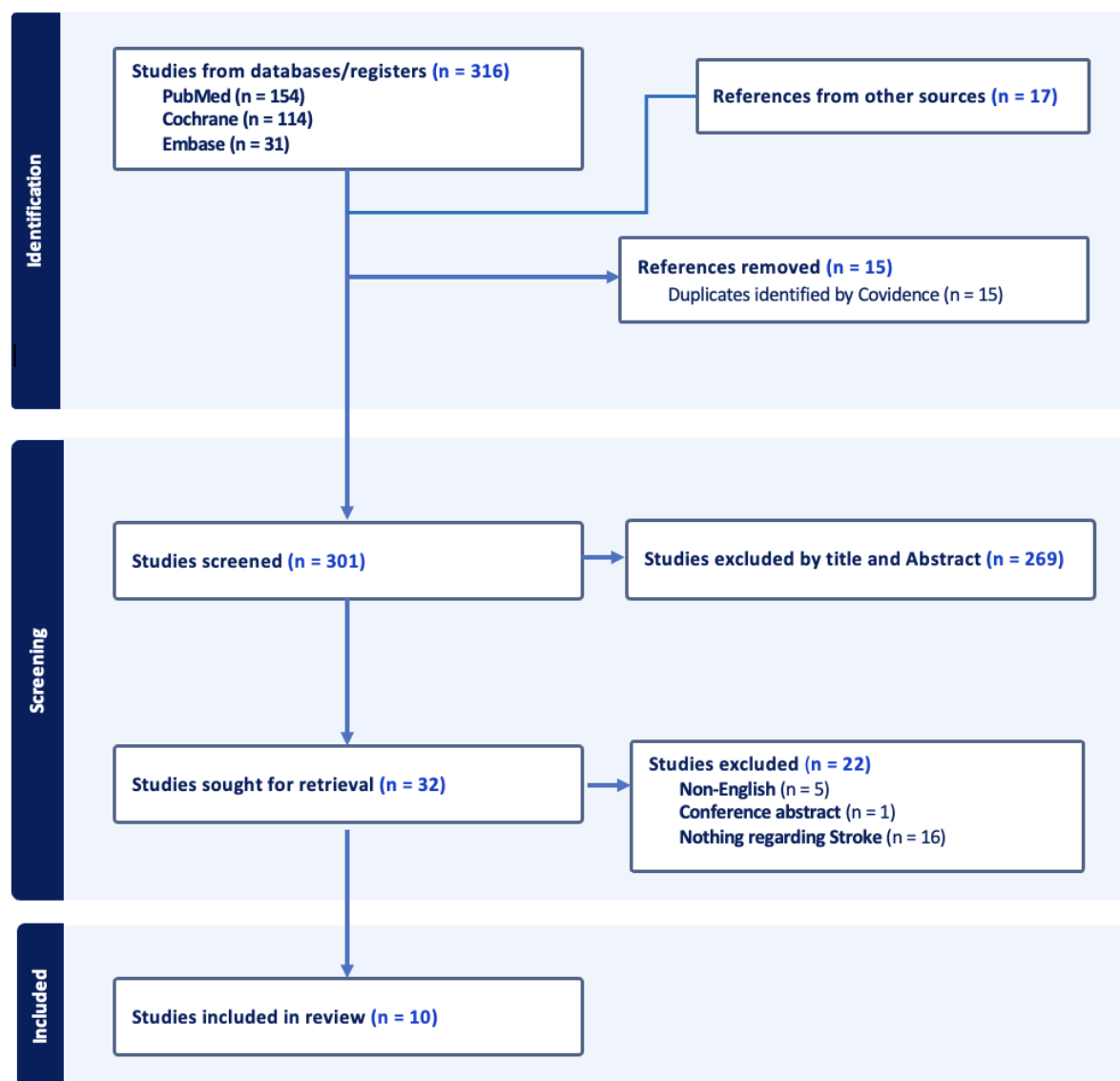


Figure 1. Flow diagram showing the identification and selection of articles in the study. A total of 301 studies were screened. Hereof, 10 studies were included.

Results

Of the 301 identified studies, 10 studies were included, comprising 1424 patients who died following a clinical stroke diagnosis, of whom 1104 patients underwent autopsy. Core areas of diagnostic discrepancy include: (1) 4 studies about under-recognition of stroke and stroke mechanisms, (2) 4 studies about missed intracranial pathology, and (3) 4 studies about systemic complications overlooked clinically (**Table 1**).

Table 1: Characteristics of the 10 studies included in the systematic review examining the correlation between clinical and neuropathological diagnoses in stroke.

Study title	Author & publication year	Study design and study setting	Mean age (years)	Study population (N)	Aim of the study	Results (Diagnostic Errors & Autopsy-Only Findings)
Sudden unexpected death caused by a stroke: A nationwide study among children and young adults in Denmark.	Frederik Nybye Ågesen et al., 2018	Retrospective nationwide mortality study, Denmark.	33 years (median)	14,567 deaths; 1,698 sudden deaths; 52 stroke-related sudden deaths. 44 autopsied.	To describe mortality rates, stroke subtype, and pre-death symptoms	Only 1/17 patients with neurological warning symptoms were suspected of stroke clinically. Of all cases, 24 patients (46%) had neurological symptoms 12 months to 24 hours before sudden death. 10 patients (19%) had neurological symptoms 1–24 hours before death. Most commonly headache in 25 (48%) of cases. 12 patients (23%) had at least one neurological symptom within one hour of death, headache remaining the most common symptom (n=9, 17%).
The frequency, causes, and timing of death within 30 days of a first stroke.	John Bamford et al., 1990	Prospective community-based cohort, Oxfordshire (UK).	Not reported.	675 patients with a first-ever stroke. 129 deaths within 30 days, 56 got an autopsy.	To determine the timing and causes of early death after stroke.	53% of deaths were attributed to the direct neurological effects of stroke, including cerebral edema and brain herniation. Among patients with cerebral infarction, 51% of deaths were caused by complications of immobility, primarily pneumonia and pulmonary embolism. Case fatality within 30 days differed by stroke subtype: 10% for cerebral infarction, 52% for intracerebral

						hemorrhage, 45% for subarachnoid hemorrhage, and 74% for strokes of uncertain pathological type.
Fatalities in a stroke unit.	Dahl T. et al., 1989	Retrospective clinical and pathological audit, Oslo City Hospital.	71.9 years	464 admitted; 24 deaths. Number autopsied: 10.	To compare the clinical cause-of-death with autopsy findings	Concordance between CT findings and autopsy was observed in 7/10 cases. In 2 cases, CT scans were normal, but autopsy revealed small cerebral infarctions, and in 1 case, CT findings interpreted as infarction or tumor were shown at autopsy to represent a brain abscess. Autopsy confirmed clinical stroke diagnosis in 6/10 cases. In 4/10 cases, discrepancies were observed between clinical vs. autopsy diagnosis in stroke patients (pneumonia vs. pulmonary embolism, brain infarct vs. brain abscess, pneumonia vs. acute myocardial infarction, cardiac insufficiency vs. pneumonia).
Diagnostic validity of fatal cerebral strokes and coronary deaths.	Anne K. Gulsvik et al., 2011	Retrospective cohort, Bergen Clinical BP Survey; linkage with autopsy data.	Not reported.	4,387 deaths. 1,140 underwent autopsy. Autopsy identified 113 fatal strokes. whereas 98 deaths were recorded as stroke in the mortality statistics.	To assess the validity of mortality statistics using autopsy	Comparison between death certificates and autopsy findings showed: - Sensitivity of stroke diagnosis: 0.75 (85/113 cases) - Positive predictive value: 0.87 (85/98 cases) - Underdiagnosed strokes: 28 cases (25%) where stroke was confirmed

at autopsy but not recorded in mortality statistics.

- Overdiagnosed strokes: 13 cases (14%) where stroke was recorded in mortality statistics but not confirmed at autopsy.

Among 28 autopsy-verified strokes that were not recorded as stroke in mortality statistics, the registered causes of death were

- Other circulatory diseases: 12 cases (including 9 ischemic heart disease)
- Pneumonia: 5 cases
- Malignant neoplasm: 4 cases- Other causes: 7 cases.

Autopsy-proven causes of in-hospital mortality in acute stroke.	Archana Hinduja et al., 2013	Retrospective autopsy study, US tertiary centre.	54 years	58 autopsies (35 full, 23 brain-only)	To identify discrepancies between clinical and autopsy diagnoses.	Complete agreement between clinical and post-mortem diagnoses was observed in 57% of cases, while 37% showed minor diagnostic discrepancies, most related to undiagnosed medical conditions such as pneumonia. 6% with major discrepancies. Autopsy-only findings – major discrepancies: - Disseminated aspergillosis in 1 patient - Ruptured iliac artery aneurysm in 1 patient - Glioblastoma multiforme causing intracerebral hemorrhage in 1 patient
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Minor discrepancies:
 - Pneumonia (often unrecognized clinically: 29% vs 49% at autopsy)
 - Pulmonary embolism identified in 2 patients at autopsy.
 - Infective endocarditis in 2 patients
 - Renal cell carcinoma in 1 patient
 - Deep venous thrombosis /renal thrombus in 1 patient

Discrepancies between clinical and autopsy findings in acute stroke.	Hudák L. et al., 2022	Retrospective autopsy study, University of Debrecen	68–75 years (median)	534 autopsies	To compare clinical vs autopsy findings	Autopsy-only findings: - Undiagnosed thromboembolism: 80 patients (15%) - Undiagnosed pneumonia: 73 patients (14% - Undiagnosed malignancies: 8 patients (2%) - Hemorrhagic transformation in 66 patients (35%) of ischemic stroke cases not seen on the last CT. Many systemic conditions were only evident at autopsy.
Diffusion MRI vs pathologically verified infarction.	Kelly P.J. et al., 2001	Combined retrospective/prospective MRI–autopsy correlation study.	60.2 years	14 autopsies	To assess the accuracy of DWI MRI vs autopsy	25 pathologically verified cerebral infarcts in autopsy. 23 of 25 infarcts detected on diffusion MRI MRI missed 2 infarcts (false negatives) and showed 2 lesions not present at autopsy (false positives) 2 patients with suspected stroke but no infarct on MRI. Overall sensitivity was 88.5% and specificity 96.6%

Early mortality following stroke.	Frank L. Silver et al., 1984	Prospective study, Sunnybrook Stroke Unit	71 years	1,073 strokes; 212 deaths. 90 autopsies (42%)	To describe the mechanisms and timing of early death	During the first week, mortality was primarily related to neurological mechanisms: - Transtentorial herniation: in 36 patients (78%) - Cardiac causes: in 7 patients (15%) - Sudden death: in 2 patients (4%) - Sepsis; in 1 patient (2%) In weeks 2–4, systemic complications became the predominant causes of death: - Pneumonia: in 28 patients (35%) - Cardiac causes: in 17 patients (22%) - Pulmonary embolism: in 4 patients (5%) - Sepsis: in 4 patients (5%)
Haemorrhagic transformation in ischaemic stroke is more frequent than suspected.	Rita Szepesi et al., 2016	Retrospective neuropathology/autopsy study	62.6 years (ischaemic subgroup)	Of the 100 patients with autopsies, 64 patients were clinically diagnosed with acute ischemic stroke and were autopsied.	To assess the autopsy value in acute stroke	In 64 patients with clinically diagnosed ischemic stroke, hemorrhagic transformation was clinically detected in 10 cases on CT-scanning (16%), while autopsy identified an additional 24 previously unrecognized cases, increasing the total to 34 cases (53%).
Autopsy-verified causes of death after stroke.	Viitanen M. et al., 1987	Prospective autopsy-based population study, Sweden	72.1 years	409 stroke patients. 224 died during follow-up. Autopsies were performed in 134 cases (61%)	To determine the true causes of death after stroke.	First week, 90% of deaths were directly attributable to the cerebrovascular lesion. Following weeks, related systemic complications became the predominant causes of death: - pulmonary embolism (30% of deaths in first 2–4 weeks)

- bronchopneumonia (27%, 2–3 months after stroke). Beyond three months, cardiac disease accounted for 37% of deaths. Overall, 59% of deaths after ischemic stroke were due to non-neurological complications,

This table summarizes the characteristics of the studies included in the systematic review, including study design, mean age (years), population (N), aim of the study, and key findings related to diagnostic discrepancies and autopsy findings. N= number, MRI = Magnetic Resonance Imaging, CT = Computed Tomography.

1. Under-recognition of Stroke - Stroke-related mechanisms

Multiple studies demonstrated that stroke was often not suspected premortem, particularly in younger individuals. Ågesen et al. identified 52 stroke-related sudden deaths, of which 44 underwent autopsy, while the remaining were verified by imaging. Among the patients who had neurological symptoms before death, stroke was clinically suspected in only 1 case, indicating substantial under-recognition of stroke as a cause of sudden death. Similarly, population-based studies of early mortality following stroke demonstrated that causes of death were frequently misattributed clinically. In the Oxfordshire Community Stroke Project, Bamford et al. reported that among 129 patients who died within 30 days after a first stroke, 10% died due to cerebral infarction, 52% due to hemorrhagic stroke, 45% due to subarachnoidal hemorrhage, and 74% were classified as having an uncertain pathological type. 53% of deaths were attributed to direct cerebral damage, predominantly in hemorrhagic stroke. In contrast, among patients with cerebral infarction, 51% of deaths were due to complications of immobility, including pneumonia and pulmonary embolism, rather than the primary brain lesion (Bamford et al., 1990).

A comparable pattern was observed in Silver et al., a prospective review, where 212 of 1073 patients (20%) died within 30 days. Transtentorial herniation (TTH) accounted for 36 deaths (78%), while brainstem extension and cerebellar compression accounted for 2 and 1 deaths, respectively. In the period beyond the first week after supratentorial stroke, deaths were mainly attributed to pneumonia (35%, n=28) and cardiac causes (22%, n=17), followed by pulmonary embolism (5%, n=4) and sepsis (5%, n=4). Additional causes included sudden death (3%, n=2), whereas 13 of 28 deaths following infratentorial infarction were classified as unknown (Silver et al., 1984).

Gulsvik et al. compared national mortality statistics with autopsy findings in 1140 deaths and identified discrepancies in cause-of-death classification. Autopsy confirmed 113 cases of fatal stroke, whereas 98 deaths had been recorded as stroke in mortality statistics. The sensitivity of registered fatal stroke diagnoses was 0.75 (85/113 cases), with a positive predictive value of 0.87 (85/98 cases). Among the 83 autopsy-verified stroke deaths, 28 cases (25%) were not recorded as strokes in the mortality statistics. In these cases, the registered causes of death included other circulatory diseases (43%, n=12), pneumonia (18%, n=5), malignant neoplasms (14%, n=4), and other causes (25%, n=7). Furthermore, deaths attributed to stroke

were associated with a lower likelihood of undergoing autopsy, indicating potential systematic bias in post-mortem verification (Gulsvik et al., 2011).

2. Missed intracranial pathology

Autopsy consistently demonstrated that clinically and radiologically undetected intracranial pathology persisted. Studies by Dahl et al. and Kelly et al. have shown that small infarcts, early ischemic changes, and brain abscesses could be masked or misinterpreted on CT or MRI (Dahl et al., 1989; Kelly et al., 2001). In the study by Dahl et al., 464 patients were admitted with stroke, of whom 24 died, and 10 underwent autopsy. Concordance between CT findings and autopsy was observed in 7 out of 10 cases. CT scans were normal in 2 cases, whereas autopsy revealed small cerebral infarctions. In 1 case, CT findings interpreted as a small infarct or possible tumor were shown at autopsy to represent a brain abscess (Dahl et al., 1989). Kelly et al. compared MRI and autopsy findings in 25 stroke patients over a 3-year period. MRI correctly identified 23 of 25 infarcts confirmed at autopsy. In 2 cases, autopsy revealed 2 small infarcts not detected on MRI. Additionally, in 2 regions diffusion MRI demonstrated signal abnormalities without corresponding infarcts on autopsy (Kelly et al., 2001) (Dahl et al., 1989).

Szepesi et al. and Hudák et al. demonstrated that hemorrhagic transformation was substantially underdiagnosed. Szepesi et al. found that hemorrhagic transformation was detected only at autopsy in 34 of 64 ischemic stroke patients (53%), while Hudák et al. reported postmortem detection in 66 of 189 cases (35%) that had not been recognized radiologically (Hudák et al., 2022; Szepesi et al., 2016).

3. Systemic complications are frequently overlooked

A major shared finding across the studies was the high rate of clinically unrecognized systemic conditions contributing to death. Autopsy uncovered pneumonia, pulmonary embolism, myocardial infarction, endocarditis, sepsis, fungal infections, and occult malignancies that were not detected clinically. In the study of Hinduja et al., 58 patients with a diagnosis of stroke died and were autopsied. Clinically unrecognized systemic conditions contributing to death were accounted for in 16 patients, mostly including pneumonia, which was suspected clinically in 29% of cases but identified in 49% at autopsy. Autopsy also revealed unrecognized pulmonary embolism (n=2), renal cell carcinoma (n=1), infective

endocarditis (n=2), and DVT/renal thrombus (n=1)(Hinduja et al., 2013). Hudák et al., which are based on 534 autopsies, similarly reported clinically unrecognized thromboembolism in 15% of cases (n=80) and pneumonia in nearly 14% (n=73). Additionally, occult malignancies were undetected premortem in 2% of cases (n=8) (Hudák et al., 2022).

Viitanen et al. and Silver et al. confirmed that systemic causes become increasingly common contributors to death in the weeks after stroke and were often misattributed clinically (Silver et al., 1984; Viitanen et al., 1987). Viitanen et al. showed in a population-based autopsy study that systemic causes of death are often dominant after the acute phase. Pulmonary embolism was a leading cause of death in the second to fourth week, seen in 30% patients, bronchopneumonia in the following months, observed in 27% of patients, and cardiac disease, particularly myocardial infarction, later after stroke – observed in 37% of patients. Importantly, death was attributed to causes other than the primary brain lesion in 59% of patients with ischemic stroke, emphasizing the major role of systemic complications in overall mortality (Viitanen et al., 1987). Silver et. al. showed that early deaths were mainly due to the direct effects of the stroke in almost 42% of the patients. However, the majority of the deaths were increasingly attributed to systemic complications in the later weeks after stroke, most notably pneumonia in 35% of the patients, cardiac causes contributing to 22% of deaths, pulmonary embolism 5%, and septicaemia 5% (Silver et al., 1984).

Discussion

This literature review synthesized the evidence from autopsy-based studies evaluating diagnostic concordance in patients with clinically suspected or confirmed stroke. Across the included studies, three consistent themes emerged: Incomplete recognition of stroke-related mechanisms, undetected intracranial pathology despite neuroimaging, and a substantial contribution of clinically unrecognized systemic complications. These findings indicate that autopsy continues to serve both as a diagnostic verification tool and as a means of improving the accuracy of cause-of-death attribution in stroke-related mortality (Viitanen et al., 1987; Hinduja et al., 2013; Hudák et al., 2022).

Autopsy findings and diagnostic discrepancies

Across the reviewed studies, discrepancies between clinical diagnoses and post-mortem findings were common. These discrepancies encompassed both incorrect classification of stroke mechanisms and failure to identify relevant intracranial or systemic pathologies. Several studies demonstrated that stroke was not suspected clinically in a proportion of patients later confirmed by autopsy, particularly in cases of sudden death or atypical clinical presentation (Bamford et al., 1990; Silver et al., 1984). Autopsy studies further demonstrated that intracranial pathology was frequently missed or misinterpreted premortem. In the CT era, Dahl et al. (1989) reported discrepancies between imaging and autopsy findings, including small cerebral infarctions not visualized on CT and a brain abscess misclassified as an infarction or tumor. With the introduction of diffusion-weighted MRI, diagnostic accuracy improved but remained incomplete. Kelly et al. (2001) demonstrated high concordance between MRI and autopsy for established infarcts, yet autopsy revealed additional small infarcts not detected on imaging and diffusion abnormalities without corresponding pathological lesions. These findings indicate that imaging-based diagnosis, while essential, does not fully substitute for pathological confirmation (Dahl et al., 1989; Kelly et al., 2001).

Hemorrhagic transformation represented a particularly important source of diagnostic discordance. Studies demonstrated that hemorrhagic transformation was frequently unrecognized premortem, despite routine neuroimaging. Szepesi et al. (2016) identified autopsy-verified hemorrhagic transformation in a substantial proportion of ischemic stroke patients, a finding corroborated by Hudák et al. (2022), who reported post-mortem detection of hemorrhagic transformation in cases without radiological evidence. These observations underscore the limitations of imaging in detecting secondary intracranial pathology and highlight the continued diagnostic value of autopsy (Szepesi et al., 2016; Hudák et al., 2022).

The findings suggest that imaging-based diagnosis may underestimate the complexity and extent of pathological processes occurring in the brain after stroke. From a clinical perspective, this highlights the inherent limitations of neuroimaging and may underscore the value of neuropathological examination in providing a more comprehensive understanding of stroke-related death. This is particularly relevant considering the growing recognition of stroke being a systemic disease with multiorgan involvement. In this context, autopsy remains an important tool for clarifying the underlying mechanisms of death, particularly in cases where the clinical cause of death is uncertain.

Systemic pathology and cause-of-death validation

A consistent finding across the included studies was the high prevalence of systemic conditions contributing to death that were not identified clinically. Autopsy frequently revealed pneumonia, pulmonary embolism, myocardial infarction, infective endocarditis, sepsis, and occult malignancies that were not diagnosed premortem (Viitanen et al., 1987; Hinduja et al., 2013; Hudák et al., 2022). These findings demonstrate that stroke-related death is often multifactorial and that patients frequently die with, rather than solely from, cerebrovascular disease. Population-based autopsy studies further clarified the temporal evolution of causes of death after stroke. Viitanen et al. (1987) demonstrated that systemic causes increasingly dominated mortality beyond the acute phase, with pulmonary embolism and bronchopneumonia emerging in the weeks following ischemic stroke and cardiac disease becoming more prominent later. Similar patterns were observed in hospital-based cohorts, where later deaths were frequently attributed to systemic complications rather than direct neurological injury (Silver et al., 1984; Bamford et al., 1990). These findings emphasize that stroke should not only be considered as a neurological disorder but as a systemic disease with multiorgan involvement. Acute cerebrovascular injury initiates a complex cascade of systemic responses, including inflammatory activation, autonomic dysregulation, and immunosuppression, which may predispose patients to complications affecting multiple organ systems. Previous studies have demonstrated that stroke is associated with increased susceptibility to infections, particularly pneumonia, as well as cardiovascular complications such as myocardial injury and arrhythmias (Balch et al., 2020; Iadecola & Anrather, 2011). In addition, stroke-induced immune alterations and systemic inflammatory responses have been shown to contribute to secondary organ dysfunction and adverse outcomes (Iadecola & Anrather, 2011). These mechanisms may partly explain the high prevalence of systemic complications identified in postmortem studies and highlight the importance of comprehensive medical management that extends beyond the primary neurological injury.

The importance of autopsy for validating cause-of-death statistics was demonstrated by Gulsvik et al. (2011), who reported substantial agreement between registered and autopsy-verified causes of death, but identified frequent misclassification in the absence of post-mortem verification. The declining autopsy rate observed over time, from roughly 40% in the 1960s to 11% after 2000, poses a risk to epidemiological validity and may lead to systematic bias in population-based data. Notably, a significant proportion of autopsy-confirmed fatal strokes were not recorded as stroke-related deaths in mortality

statistics, indicating that reliance on clinical certification alone may introduce systematic bias.

Methodological considerations and potential limitations

Interpretation of the findings is limited by heterogeneity among the included studies in design, populations, diagnostic definitions, and autopsy practices. Autopsy rates varied substantially across studies over time, and post-mortem examination was not performed systematically, introducing potential selection bias. Differences in definitions of diagnostic discrepancy and cause-of-death attribution further limit direct quantitative comparison across studies (Viitanen et al., 1987; Hudák et al., 2022).

Advances in neuroimaging and stroke management during the study periods may also have influenced diagnostic concordance, complicating comparisons between earlier and more recent cohorts. In addition, non-English studies were excluded, which may have resulted in the omission of relevant evidence. In several studies, documentation of premortem neuroimaging was incomplete, limiting assessment of imaging–autopsy concordance. Consequently, these limitations do not detract from the consistent observation across studies that autopsy provides clinically meaningful diagnostic clarification in stroke-related deaths.

All postmortem examinations included in this review were hospital-based clinical autopsies; no forensic autopsy series were included. Clinical and forensic autopsies are undertaken under different indications and are consequently subject to distinct selection mechanisms. However, this distinction was not considered to materially affect the primary objective of the review, which was to evaluate discrepancies between premortem clinical diagnoses and postmortem pathological findings in stroke-related deaths.

Implications for future research and clinical practice

Given the ethical, cultural, and economic constraints limiting routine autopsy, future research should focus on identifying clinical scenarios in which post-mortem examination yields the greatest diagnostic benefit. Selective autopsy of patients with atypical clinical courses, unexpected death, or diagnostic uncertainty may optimize resource utilization while preserving the diagnostic, educational, and epidemiological value of autopsy (Burton & Underwood, 2007).

From a clinical quality-assurance perspective, autopsy remains a valuable means of identifying diagnostic blind spots, particularly in cases of uncertain imaging findings or unexpected deterioration (Dahl et al., 1989; Hinduja et al., 2013). In settings where full autopsy rates have declined, partial or targeted autopsies may still provide useful information, although they may underestimate systemic pathology (Hudák et al., 2022). Structured clinico-pathological correlation meetings could further enhance diagnostic accuracy and education, as previously advocated in stroke cohorts (Viitanen et al., 1987; Ågesen et al., 2018).

Educational implications and declining autopsy rates

Beyond its diagnostic value, autopsy also plays an important educational role in medical training. The global decline in autopsy rates has raised concerns regarding reduced opportunities for pathologists and clinicians to maintain and develop diagnostic expertise. Academic pathology programs increasingly report difficulties in providing sufficient autopsy material for trainees, potentially affecting both training quality and continued professional competence (Shojania & Burton, 2004). The declining rate of autopsies and the resulting reduction in the educational training for pathologists are likely to become a weak point in the field of stroke. This is particularly important because autopsy findings provide added value by revealing conditions that might otherwise remain undetected.

Conclusion

Autopsy-verified studies demonstrate that, despite major technological progress, important diagnostic discrepancies persist in patient cohorts who have died from a stroke. Autopsy remains a valuable tool and golden standard for diagnostic clarification in stroke patients by identifying clinically unrecognized pathology, such as systemic complications, and correcting misclassified causes of death, despite advances in neuroimaging and clinical assessment. Autopsy should be considered if the cause of death and stroke etiology are not certain or is atypical.

Ethical approval

None.

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None.

Conflict of interest

None.

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