ASIAN ARCHIVES OF PATHOLOGY

THE OFFICIAL JOURNAL OF THE ROYAL COLLEGE OF PATHOLOGISTS OF THAILAND

Volume 6
Number 4
October – December 2024

INDEX COPERNICUS INTERNATIONAL

Print ISSN: 1905-9183
Online ISSN: 2673-0499

EDITORIAL BOARD

ABOUT THE JOURNAL

Aims and Scope

Asian Archives of Pathology (AAP) is an open access, peer-reviewed journal. The journal was first published in 2002 under the Thai name "วารสารราชวิทยาลัยพยาธิแพทย์แห่งประเทศไทย" and English name "Journal of the Royal College of Pathologists of Thailand". The journal is a publication for workers in all disciplines of pathology and forensic medicine. In the first 3 years (volumes), the journal was published every 4 months. Until 2005, the journal has changed its name to be "Asian Archives of Pathology: The Official Journal of the Royal College of Pathologists of Thailand", published quarterly to expand the collaboration among people in the fields of pathology and forensic medicine in the Asia-Pacific regions and the Western countries.

The full articles of the journal are appeared in either Thai or English. However, the abstracts of all Thai articles are published in both Thai and English languages. The journal features letters to the editor, original articles, review articles, case reports, case illustrations, and technical notes. Diagnostic and research areas covered consist of (1) **Anatomical Pathology** (including cellular pathology, cytopathology, haematopathology, histopathology, immunopathology, and surgical pathology); (2) **Clinical Pathology (Laboratory Medicine)** [including blood banking and transfusion medicine, clinical chemistry (chemical pathology or clinical biochemistry), clinical immunology, clinical microbiology, clinical toxicology, cytogenetics, parasitology, and point-of-care testing]; (3) **Forensic Medicine (Legal Medicine or Medical Jurisprudence)** (including forensic science and forensic pathology); (4) **Molecular Medicine** (including molecular genetics, molecular oncology, and molecular pathology); (5) **Pathobiology**; and (6) **Pathophysiology**.

All issues of our journal have been printed in hard copy since the beginning. Around the late 2014, we developed our website (www.asianarchpath.com) in order to increase our visibility. We would like to acknowledge that our journal has been sponsored by the Royal College of Pathologists of Thailand. We have the policy to disseminate the verified scientific knowledge to the public on a non-profit basis. Hence, we have not charged the authors whose manuscripts have been submitted or accepted for publication in our journal.

On the other hand, if any authors request a printed copy of the journal issue containing the articles, each of the copied journals costs 450 baht for Thai authors and 30 United States dollars (USD) for international authors.

Publication Frequency

Four issues per year

Disclaimer

The Royal College of Pathologists of Thailand and Editorial Board cannot be held responsible for errors or any consequences arising from the use of information contained in Asian Archives of Pathology. It should also be noted that the views and opinions expressed in this journal do not necessarily reflect those of The Royal College of Pathologists of Thailand and Editorial Board.

MANUSCRIPT REVIEWERS

CONTENTS

ORIGINAL ARTICLE

THE ESSENCE OF THE POSTMORTEM EXAMINATION IN THE EVALUATION OF ANTEMORTEM DIAGNOSTIC DISCREPANCIES AND MEDICAL ERRORS

Oluwagbenga Tosin ALADE[1], Akinwumi Oluwole KOMOLAFE[2*] and William Olufemi ODESANMI[2]

1 *Ekiti State Hospitals Management Board, Ekiti State.*

2 *Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State.*

* Correspondence to: Akinwumi O. Komolafe. Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria. Email: akinkomo1@yahoo.com Mobile Phone/WhatsApp number: +234 8033557741

Conflict of interest: The authors declare that they have no conflicts of interest with the contents of this article.

Submitted: *8 March 2023*
Accepted: *24 March 2023*
Published: *1 December 2024*

Abstract

The incidence of antemortem diagnostic errors during clinical management is unbelievably high and this is worrisome. Many of these cases were undetected and resulted in disease progression and fatal outcome, necessitating autopsies. The postmortem examination continues to play an enviable, foremost and pivotal role as the gold standard in unraveling circumstances surrounding deaths emanating from patients' management. Major diagnostic discrepancies were detected in 39 patients (42.2%), of these 39 patients, 17 cases (42.5%) were attributed to the sequelae of systemic hypertension, 12 cases (30.0%) were due to infections, 7 cases (17.5%) were due to neoplasms and 3 cases were due to gastrointestinal diseases. Eighteen 18 patients (45.0%) out of the 39 patients were classified as class I, and 21 patients (52.5%) classified as class II. Minor diagnostic discrepancy (class III; IV) was identified in 16 patients. Minor discrepancies were identified in 12 patients with a major error as well. Thus, an overall number of 28 patients with minor discrepancies were identified. Of these 28 patients, 19 patients (65.5%) were classified as class III and 9 patients (31.0%) were classified as class IV (see table 6). In 53 patients (57.0%) the clinical diagnoses were in complete agreement with the autopsy findings and were classified as class V.

The most frequently observed class I major discrepancies were due to the complications of systemic hypertension such as pulmonary oedema, biventricular heart failure and acute left ventricular failure. The most commonly observed class II major discrepancies were neoplasms, gastrointestinal complication, infections, cerebrovascular complications and cardiac complication. The most commonly observed class III minor discrepancies were renal complications, cardiac complications, neoplasms and GIT/liver complications, while class IV minor errors were urogenital complications, gastrointestinal/liver complications, respiratory complication and musculoskeletal complications.

Confirmation of diagnostic discrepancies can only be absolutely proven by postmortem examination. The Goldman's criteria offer a fair approach for ascertaining the degree of deviation of antemortem diagnoses from autopsy diagnoses.

Keywords: postmortem evaluation, antemortem diagnostic discrepancies, medical errors

Introduction

Diagnostic discrepancies are fairly common challenges encountered in routine medical care. They are medical errors of varying severity and deviations encountered in the diagnostic process with far-reaching medicolegal implications [(1)]. Such misses could evoke questions about the antemortem management of the deceased. The fear of medical litigations precludes the request for autopsies by clinicians [(2-3)]. Since patients must go through a process of diagnoses before appropriate care is implemented, it becomes imperative to subject the patient to a process of systematic interview or clerking, a process which interrogates diligently the evolution of the clinical features that is the symptoms and signs, critically observes patients during physical examination with a mental processing of the possible differential

diagnoses before deciding or provisional clinical diagnoses with a view to developing a management plan which entails the set of relevant investigations before actual treatment. Failure to ask relevant questions during history taking or conduct thorough relevant physical examination, misinterpretation of results, presumptuous empirical treatments that altered the pathogenesis or pathophysiology of diseases may contribute to errors of judgement. It is imperative to have a model to classify the degree of deviation from the actual clinical diagnosis after a postmortem diagnosis is made. The study is aimed at using the Goldman's classification as a basis of ascertaining the degree of deviation between the clinically documented antemortem diagnosis and the actual antemortem diagnosis revealed at the autopsy.

Aims and Objectives

1. To ascertain the postmortem diagnoses that were discordant with antemortem diagnoses
2. To classify the degree of the discordance, using the Goldman's criteria.

Materials and Methods

This was a prospective study of all complete adult clinical autopsies including macroscopic and microscopic examination performed at the Department of Morbid Anatomy and Forensic Medicine between January 2020 and December 2020. The patient's biodata (name, age, gender) and clinical diagnoses are noted. The antemortem clinical and postmortem diagnosis were compared based on Goldman criteria for autopsy discrepancies.

Goldman's Criteria for Autopsy Discrepancies [(4)].

Major discrepancies	
Class I	Missed major diagnosis with potential adverse impact on survival and that would have changed management.
Class II	Missed major diagnosis without potential impact on survival and that would not have changed management.
Minor discrepancies	
Class III	Missed minor diagnosis related to terminal disease but not related to the cause of death.
Class IV	Missed minor diagnosis not related to terminal disease and cause of death but of possible epidemiology or genetic importance.
Class V	Clinical and autopsy diagnosis in complete agreement.

Results

Major diagnostic discrepancies were detected in 39 patients (42.2%), of these 39 patients, 17 cases (42.5%) were attributed to the sequelae of systemic hypertension, 12 cases (30.0%) were due to infections, 7 cases (17.5%) were due to neoplasms and 3 cases were due to gastrointestinal diseases. Eighteen 18 patients (45.0%) out of the 39 patients were classified as class I, and 21 patients (52.5%) classified as class II. (See table 1). Minor diagnostic discrepancy (class III; IV) was identified in 16 patients. Minor discrepancies were identified in 12 patients with a major error as well. Thus, an overall number of 28 patients with minor discrepancies were identified. Of these 28 patients, 19 patients (65.5%) were classified as class III and 9 patients (31.0%) were classified as class IV. In 53 patients (57.0%) the clinical diagnoses were in complete agreement with the autopsy findings and were classified as class V.

The most frequently observed class I major discrepancies attributed to complication of systemic hypertension were cardiopulmonary complication (pulmonary oedema) (n=9) and cardiac complication (biventricular heart failure and acute left ventricular failure) (n=8) while infection was seen in one case. The most commonly observed class II major discrepancies were neoplasms (n=7), gastrointestinal complication (n=2), infections (n=3), cerebrovascular complication (n=1) and cardiac complication (n=1). The most commonly observed class III minor discrepancies were renal complication (n=6), cardiac complication (n=3), neoplasm (n=4) and GIT/liver complication (n=6) while class IV minor errors are urogenital complication (n=3), gastrointestinal/liver complications (n=4), respiratory complication (n=1), musculoskeletal complications (n=1) (See table 5). Overall, it was observed that a number of cases with minor errors overlapped the major missed errors and class V of Goldman classification (See figure 1).

Table 1. Shows class I and class II Goldman classification

Class I and Class II	Discrepancies		
			No
	Cardiac complications (n=8)	Biventricular heart failure	5
		Acute left ventricular failure	3
	Cardiopulmonary complications (n=9)	Pulmonary oedema	9
Class I	Infections (n=1)	Bronchopneumonia	1
	Neoplasms (n=7)	Non-Hodgkin Lymphoma	2
		Ovarian carcinoma	1

		Colorectal carcinoma	1
		Pancreatic carcinoma	2
		Renal carcinoma	1
	Infections (n=3)	Lobar Pneumonia	1
		Disseminated Tuberculosis	2
		Peritonitis	
Class II			
	Gastrointestinal complications (n=2)	Gastric bleeding ulcers	2
	Cardiac complications (n=1)	Myocardial infarction	1
	Cerebrovascular Complications (n=1)	Subarachnoid haemorrhage	1

Table 2. Showing the class III and class IV of Goldman Classification

Class III and Class IV	Discrepancies		
			No
	GIT/Liver complications (n=6)	Liver cirrhosis	1
		Duodenal ulcers	3
		Diverticulosis	2
Class III			
	Cardiac complications (n=3)	Hypertensive Heart Disease	3
	Renal complication (n=6)	Chronic pyelonephritis	4
		Diabetes Mellitus glomerulosclerosis	2
	Neoplasms (n=4)	Prostatic carcinoma	1
		Ovarian teratoma	1
		Pancreatic carcinoma	2

	GI/Liver complications (n=4)	Asymptomatic gallstones	3
		Colonic Polyps	1
	Urogenital complications (n=3)	Benign Prostatic Hyperplasia	2
		Hydronephrosis	1
Class IV			
	Respiratory Complications (n=1)	Atelectasis	1
	Musculoskeletal Complications (n=1)	Cellulitis	1

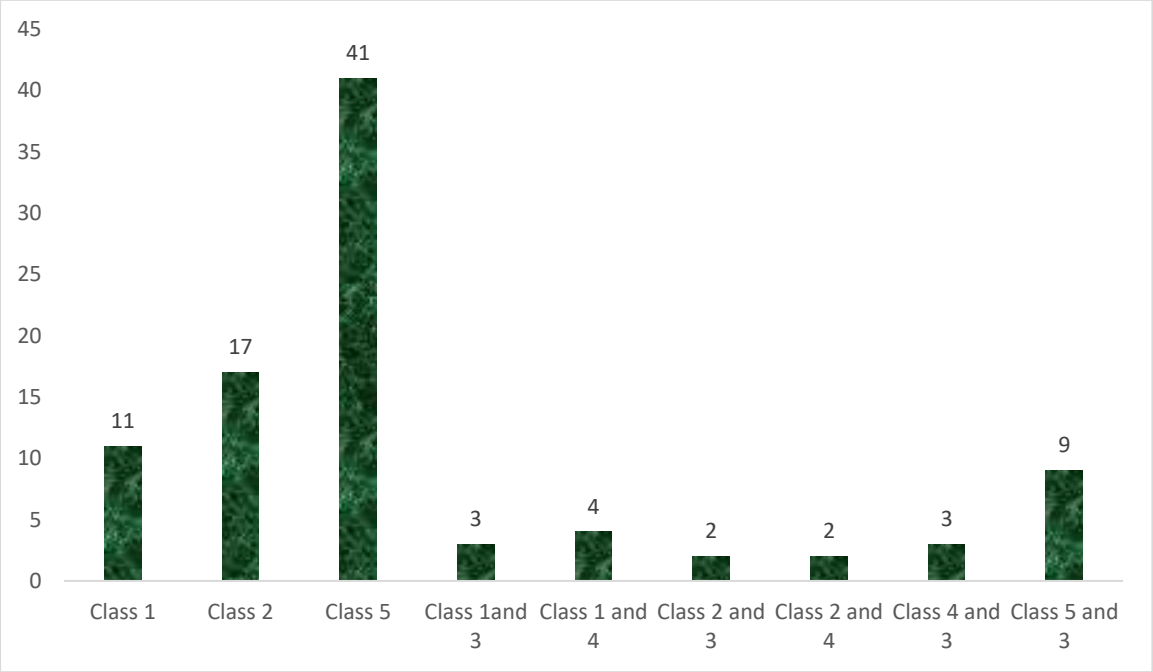

Figure 1. Shows the Goldman classification with overlapping of the minor missed errors with the major missed errors and class V.

Discussion

Our study sought to evaluate the diagnostic discrepancies and medical errors based on the Goldman's criteria. Unfortunately, not many authors or works have been done with direct reference to the Goldman's classification scheme. This may be due to the fading autopsy practice and culture in the western world and the potentially damaging outcomes of autopsy findings as they may unwittingly excavate suboptimal management secrets bordering

on medical negligence and malpractice with damning and unwholesome medicolegal consequences.

In our study, according to Goldman's classification or antemortem diagnoses versus postmortem diagnoses, 18 cases were classified as class I major missed discrepancy with cardiopulmonary complication: pulmonary oedema accounting for the largest entity. Combes et al recorded similar incidence in their study occurring in 48 cases more than what obtains in this study [5]. In another study by Kandy et al, the non–infectious cases ranked highest with cardiopulmonary diseases being the highest [6]. In this study class II major missed discrepancies was higher than class I major missed discrepancies. This was similar to study done by O'Connor et al. [7] where class I was as low as 4 cases and class II was more preponderant. Silas et al. [9] in north-central Nigeria reported a deviation in their study where class I missed major diagnosis surpassed the class II missed major diagnosis. The most frequently encountered class II discrepancies were malignant neoplasms including non-Hodgkin lymphoma, ovarian, colorectal, pancreatic and renal carcinoma. Class III missed minor discrepancies in this study overlapped class I, class II and class V and was in 19 patients. The most frequently observed were liver cirrhosis, duodenal ulcers and diverticulosis. Class IV also overlapped class I, class II and class III with the most missed being asymptomatic gallstones and colonic polyps. This study showed that missed minor discrepancies exist and can only be discovered with full and thorough autopsy with microscopic examination even though it's been argued that postmortem imaging modalities can also reveal these lesions.

Coradazzi et al in their series reported that the 50% of clinical diagnosis were not suspected and listed missed cases of venous thromboses (83%), pulmonary embolisms (80%), bronchopneumonias (46%) and neoplasia (38%) [8]. Coradazzi et al found iatrogenic injuries to be quite frequent but unfortunately approximately 90% of the cases were not documented in clinical reports [8]. We posit that the management team may have been done deliberately to avoid implicating the managing team in order to avoid medicolegal challenges.

A strong accord was found between the clinical diagnoses rendered before death by the clinician and autopsy findings in patients who died during their hospitalization. This is not far from the findings by Onwuezobe et al9 in Niger Delta Nigeria and Pakis et al. [10] Spiliopoulou et al in Greece presented a poor congruity between the clinical diagnosis and autopsy findings in their study [11]. We observed that the concordant rate was common among the male gender and seen more in the middle age group which is similar to the findings of Spiliopoulou et al. [11], although Veress and Alafuzoff reported a contrast results in their studies [12].

From this study a few observations were made in a bid to explain the frequency of concordance and/or the discrepancy discovered. It was observed that clinicians only request for autopsies in cases that are clinically challenging or difficult to resolve and did not request for autopsies when they are so sure of the clinical diagnosis. In addition, clinicians issue death certificates for cases that ordinarily would have been autopsied due mostly to either the level

of confidence in the diagnosis or avoiding diagnostic errors that may be perceived as problematic. It was assumed that these unstudied cases would have improved the concordance rate were autopsies done. In separate studies by Hartveit and Britton, they reported that autopsy changes clinical diagnosis in cases in which the clinician were very confident about the cause of death and that the rate increased in cases where the clinicians were unsure of the diagnosis [13-14]. This only showed that autopsy alone can refute diagnosis and can uphold diagnosis.

Hyejong et al identified 9.9% cases as class I discrepant diagnoses with a potential significant impact on survival or treatment [15]. They also found critical findings, such as untreated infection in 45.5%, pulmonary embolism 24.2%, and undiagnosed malignancy 18.2% of their cases [15]. Hyejong further noted that major significant findings that were not clinically detected antemortem and consistent with class I and class II, whether clinically manageable or not (class I and II), were found in 19.5% [15]. Tejerina et al found significant discrepancies in 18.5% of patients who underwent autopsy, 7.5% of them were diagnoses which if made antemortem and appropriately managed would have had positive impact on both the therapy and outcome [16].

Komolafe et al in their study bemoaned the seemingly high burden of missed diagnoses particularly because many of the cases of medical errors in their series are common ailments in their environment of practice, are usually easily diagnosable cases and were potentially treatable benign conditions if they had been diagnosed to prevent the fatal outcomes. Baker also found major diagnostic errors in 39.7% and minor diagnostic errors in 17.3% of autopsies which contributed to the deaths of patients in both circumstances [17]. Britton in the University Hospital in Stockholm, Sweden found undiagnosed main cause of death in 43% of the autopsies [14]. This is also unacceptably high considering the standard of practice expected of the hospital and the expected expertise of the personnel. David et al in a systematic review also noted that autopsies discovered 23.5% of clinically missed diagnoses involving principal or underlying cause of death as well as 9% of errors that would or could have changed positively the outcome for the patient [18]. It is noteworthy to state that the problem wrong, misdiagnoses and diagnoses, erroneous summations and wrong judgment in clinical management does not exclude any professional cadre or practice setting, no matter the technological advancement of the hospital, profile of the personnel involved. Perhaps, the fallibility of man makes him vulnerable to errors in cases with atypical presentations or falls short of his experience. Casali et al ascertained medical errors in 17% of cases; in their postmortem evaluation of suspected malpractice, 50% of which were surgical mistakes [19]. However, Madae et al in his autopsy series found a lower figure of 4.24% deaths due to medical errors in suspected malpractice cases [20]. Sonderegger-Iseli et al also found 10-20% of major unexpected discrepancies cum diagnostic errors that would have changed the management of patients.

Our study showed that infections were not likely to be missed or misdiagnosed. There were only two cases of disseminated tuberculosis and cellulitis. This is in sharp contrast to the work of Komolafe et al in which infections such as pulmonary tuberculosis, acute pyelonephritis, typhoid enteritis, pyogenic meningitis and lobar pneumonia were not diagnosed with resultant fatality of the cases. Akinwusi et al also showed the various contributions of variable infections to death as seen in their study in which typhoid septicaemia was responsible for sudden death in 47.1%, and lobar pneumonia in 17.7%, pulmonary tuberculosis in 17.7% of patients respectively [(21)]. perhaps the difference might be explained why better disease surveillance, diagnostic technique and management in our heaty facility, particularly with growing expertise, training and technical support in recent years. Our findings also showed that complications of systemic hypertension were missed with resultant fatality. Our findings are well supported by that of Akinwusi et al who found that in their work on sudden deaths, systemic hypertension-related causes accounted for 48.3% of sudden deaths [(22)]. It is however quite pertinent to state that missing systemic hypertension and its complications in cases affecting a predominantly black population have worrisome implications of the general care of patients and medicolegal implications.

Our study shows a universal occurrence of discrepancies between clinical and autopsy diagnoses with higher frequencies of Goldman I and II classes of discrepancies, suggesting that highly sensitive and specific diagnostic hi-tech tests though necessary and informative cannot always substitute for the basic elements of wholehearted interaction with patients through thorough clerking, diligent observation during clinical examination, correlation of the results of investigations with clinical picture, resisting attempts to gloss over atypical presentations, which indeed may be red flags to reconsider our diagnoses.

Conclusion

The Goldman's classification of diagnostic discordance and concordance between antemortem clinical and postmortem diagnoses is a fair way of stratifying the degree of deviation of the discrepancies or conformity.

The study further exemplifies the role of the autopsy in the detection of misdiagnosis and missed diagnoses, which no doubt has medicolegal implications in pursuing claims related to medical negligence and malpractice. Since the autopsy remains the only means of ascertaining most precisely the antemortem events, proactive structures should be put in place to request, perform postmortem examination and document the findings systematically with diligent clinicopathological correlations with the results of investigations done antemortem with a bid to correcting wrong interpretation of antemortem tests' results,

improving diagnostic skills and consolidating on professional competence. Thus, structures should be put in place to conduct autopsies on clinical deaths statutorily, especially when deaths occur in inexplicable circumstances. Findings garnered from the exercise would be invaluable revelations that would make physicians wiser and better prepared for the next patient and prevent future medicolegal challenges cum embarrassment. The postmortem examination remains highly crucial in confirming antemortem diagnostic accuracy and the knowledge of findings and experience has invaluable potentials in improving the quality of care of patients. Though fast becoming unpopular due to over-reliance on modern diagnostic techniques, the autopsy consult may help to reduce compensation for damages should autopsy findings exculpate the managing team and the hospital.

References

(1). Komolafe AO, Adefidipe AA, Akinyemi HAM, et al. Medical Errors Detected at the Autopsy: A Prelude to Avoiding Malpractice Litigations. J Adv Med Med Res 2018; 27: 1 – 8.

(2). Gartland RM, Myers LC, Iorgulescu JB, et al. Body of evidence: Do autopsy findings impact medical malpractice claim outcomes? J Patient Saf 2021; 17: 576 – 82.

(3). Oyebode F. Clinical errors and medical negligence. Med Princ Pract 2013; 22: 323 –3.

(4). Lee Goldman, Staney Robbins LH. The value of autopsy in three medical eras (1983) artículo clave inicial. New Engl J Med 1983; 308: 1000 – 5.

(5). Combes A, Luyt CE, Trouillet JL, et al. Is there still a role for autopsies in the intensive care unit? Clin Pulm Med 2006; 13: 188 – 93.

(6). Kandy NC, Pai MR, T RP, et al. Role of Histopathology On Autopsy Study: An Audit. SAS J Med. 2015; 1: 7 – 15.

(7). O'Connor AE, Parry JT, Richardson DB, et al. A comparison of the antemortem clinical diagnosis and autopsy findings for patients who die in the emergency department. Acad Emerg Med 2002; 9: 957 – 9.

(8). Coradazzi AL, Morganti ALC, Montenegro MRG. Discrepancies between clinical diagnoses and autopsy findings. Braz J Med Biol Res 2003; 36: 385 – 91.

(9). Ekpo MD, Abudu EK, Umanah IN OI. An audit of medical autopsy: experience at the University of Uyo Teaching Hospital (UUTH), Niger Delta region, Nigeria. Indian J Med Sci 2013; 65: 502 – 9.

(10). Pakis I, Polat O, Yayci N, et al. Comparison of the Clinical Diagnosis and Subsequent Autopsy Findings in Medical Malpractice. Am J Forensic Med Pathol 2010; 31: 218 – 21.

(11). Spiliopoulou C, Papadodima S, Kotakidis N, et al. Clinical diagnoses and autopsy findings: A retrospective analysis of 252 cases in Greece. Arch Pathol Lab Med. 2005; 129: 210 – 4.

(12). Veress B, Alafuzoff I. A retrospective analysis of clinical diagnoses and autopsy findings in 3,042 cases during two different time periods. Hum Pathol 1994; 25: 140 – 5.

(13). Hartveit F. Journal of. Clinical and post-mortem assessment of the cause of death. J Pathol 1977; 123: 193 – 210.

(14). Britton M. Diagnostic errors discovered at autopsy. Acta Med Scand 1974; 196: 203 – 10.

(15). Marshall HS, Milikowski C. Comparison of clinical diagnoses and autopsy findings: Six-year retrospective study. Arch Pathol Lab Med 2017; 141: 1262 – 6.

(16). Tejerina E, Esteban A, Fernández-Segoviano P, et al. Clinical diagnoses and autopsy findings: Discrepancies in critically ill patients. Crit Care Med 2012; 40: 842 – 6.

(17). Dellefield ME, Kelly A, Schnelle JF. Quality Assurance and Performance Improvement in Nursing Homes. J Nurs Care Qual 2013; 28: 43 – 51.

(18). Davies DJ, Graves DJ, Landgren AJ, et al. The decline of the hospital autopsy: A safety and quality issue for healthcare in Australia. Med J Aust. 2004; 180: 281 – 5.

(19). Casali MB, Mobilia F, Sordo S Del, et al. The medical malpractice in Milan-Italy. A retrospective survey on 14 years of judicial autopsies. Forensic Sci Int 2014; 242: 38 – 43.
(20). Madea B. Medico-legal autopsies as a source of information to improve patient safety. Leg Med 2009; 11: S76 – 9.
(21). Akinwusi PO, Komolafe AO, Olayemi OO, et al. Communicable disease-related sudden death in the 21st century in Nigeria. Infect Drug Resist 2013; 6: 125 – 32.
(22). Akinwusi PO, Komolafe AO, Olayemi OO, et al. Pattern of sudden death at Ladoke Akintola university of technology teaching hospital, Osogbo, South West Nigeria. Vasc Health Risk Manag 2013; 9: 333 – 9.

ORIGINAL ARTICLE

Characteristics of pulmonary contusions and associated thoracic injuries in direct and velocity-related blunt chest trauma: A study of gross and histopathology from autopsy

Nattanan Sirisopon and Nitikorn Poriswanish*

Department of Forensic Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand 10700

Department of Forensic Medicine, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand 10300

* Correspondence to: Nitikorn Poriswanish, Department of Forensic Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Rd., Bangkok-noi, Bangkok, Thailand 10700 Tel.: 02 419 6547-8 Email: nitikorn.por@mahidol.ac.th

Conflict of interest: The authors have no competing interest to declare.

Submitted: *21 April 2023*
Accepted: *28 April 2023*
Published: *1 December 2024*

Abstract

Background: Severe pulmonary contusions can lead to rapid or delayed mortalities. Several studies of histopathology have been performed in animal models, but there are very few in human.

Objective: This study is aimed to study both gross and histopathology of lung contusion in blunt chest trauma mainly focusing on direct and velocity-related impacts (DI and VI)

Materials and Methods: This study was a retrospective review of medico-legal autopsy reports, pictures and H&E-stained histopathological slides conducted between 2020 to 2021.

Results: Hilar lung contusion in association with tear of isthmus aorta could be good characteristics to infer that the mechanism of VI rather than DI. Conversely, injuries of tracheobronchial tree, heart, and proximal aorta tend to be from DI than VI. Histopathological dating shows that PMNs have been presented since the first 3-hour post-traumatic interval (PTI) followed by other inflammatory cells and might end up with organizing pneumonia develop after the first week in those with ARDS. Thrombosis can be found from 9-hour to 7-day PTI.

Conclusion: DI harbors some gross characteristics to distinguish from VI. The histopathological sequence ranging from 1 hour to 30 days PTI show the findings explainable by the previous animal studies in animals and could be useful for dating.

Keywords: Pulmonary contusion, Blunt chest trauma, Histopathology of pulmonary contusion, Mechanisms of pulmonary contusion

Introduction

Pulmonary contusions occur of around 25-80% of blunt chest trauma which may be seen isolated or associated with other injuries [(1)]. The highest incidence of pulmonary contusion is from traffic accidents [(2)]. Approximately 20-22% of patients suffered from blunt chest trauma could be detected signs of pulmonary contusion within the first 24 hours post-traumatic interval (PTI) [(3)]. Wide variety of symptoms are from asymptomatic to acute respiratory failure [(4)].

The mechanisms of pulmonary contusion have been proposed to be generated by direct impact between the chest wall and lungs, abrupt deceleration of the lung, and explosion of lung gas and fluid [(4-6)]. In motor accidents, there have been further identified three predictive factors associated to pulmonary contusions [(7)]. The first one is an abrupt change in velocity of over 45 mph; the second one is a frontal collision to stationary object; and the last one is a near-side lateral impact [(7)].

As a consequence of different mechanisms, different gross pathology could happen. This study is to observe pathological patterns to help infer the specific mechanism of pulmonary contusion according to two main etiologies, direct crushing of the chest and velocity-related trauma.

Moreover, several studies in animal models have been performed to examine histopathological sequence and biochemical response in pulmonary contusion. To date, it seems to have very few or no previous literature performing a histopathological study in human. Therefore, this study is aimed to collect autopsied tissues from the individuals who can survive in different period of time to identify how the pulmonary contusion changes in a micro-level.

Materials and Methods

Study population

This study was a retrospective review of medico-legal autopsy reports, pictures and H&E-stained histopathological slides that were conducted at the Department of Forensic Medicine, Siriraj Hospital, Bangkok during January 2020 to December 2021. All of the cases must contain pulmonary contusions as well as being in adult age, i.e. 18 years onwards, with

evidences or clear histories of blunt chest trauma. The study was ethically approved by the Institutional Reviewing Board.

Gross pathological study

The cases recruited must contain clear histories of the mechanisms of trauma of the chest for either of the group, namely direct impact (DI), e.g. hits or compressions, and velocity-related impact (VI), e.g. traffic accidents or fallings. Those with mixed mechanisms were excluded. For the VI group, those with evidences of chest wall fractures, open wounds of the chest wall including iatrogenic operations were also excluded.

Data collection for gross pathology

Sexes, ages, weights and heights, underlying diseases, histories of event, post-traumatic intervals (PTI), and causes of death were recorded. Data were obtained about presence of external wounds on chest wall, locations of chest wall fracture in the DI group and pulmonary contusion as well as other associated intrathoracic injuries including injuries of the heart, thoracic aorta and bronchial tree. Details of location of pulmonary contusion were based on sides and lobes in accompany with broad anatomical positions, i.e. anterior, posterior, and hilar.

Ages were categorized into 6 subgroups by decades starting from ≤20 to >60 years. Weights and heights were transformed into Body Mass Index (BMI) and were categorized into 5 subgroups according to WHO (2004) [(8)]. Severities of the chest trauma were categorized by Abbreviated Injury Scale (AIS) version 2005: update 2008[(9)] focusing only for the body region 3 (AIS-BR3), and were selected to this study for those containing score ≥3 because the lower contain no lung contusion.

To correspond between locations of rib fracture and pulmonary contusion in the DI group, this study used anatomical landmarks of thoracic surgery as described in Sayeed and Darling (2007) [(10)]. They then were scored as “0” for non-concordance, “1” for < 50% concordance, “2” for ≥50% to <100% concordance, and “3” for perfect concordance.

Statistical analysis of gross pathology

Comparison of presence of external wounds, injuries of the heart-aorta-bronchial tree, and rib fracture-pulmonary contusion concordance scores within subgroups of age, BMI, and AIS were statistically analyzed by Chi square and Fisher’s exact tests through the online platform, available at https://astatsa.com/FisherTest/. Statistical significance was considered when $p < 0.05$.

Histopathological study

The victims presented with pulmonary contusions regardless of mechanisms of trauma of the chest were recruited from the autopsy cases only performed in 2021. Histopathological slides stained with H&E were selected from the victims who survived from 1 hour to over-a-week PTI as observed apparent changes in the previous studies [3,6]. Studied population overlapped those in the gross pathological study if their PTIs were over one hour. PTIs were divided into 6 groups consisting of 1-6, >6-12, >12-24, >24-72, >72-168, and >168 hours. Histopathology sequences were recorded and described according to each PTI. Numbers of cases in six PTI subgroups were shown in Table 3.

Results

Gross pathological study

A total of 103 cases out of 3,814 autopsies that were matched with the study criteria were selected. Of these, thirty-five cases were categorized as the DI group while sixty-eight cases were found to be belonged to the VI group. Ages in DI were ranged from 21 to 76 years (median 39 years) while those in VI were ranged from 18 to 63 years (median 25.5 years). BMIs in DI were ranged from 17.1 to 47.5 (median 23.4) while those in VI were ranged from 17.0 to 38.4 (median 22.3). Distributions of sex, age, BMI, and AIS-BR3 of both groups were presented in Table 1.

The major causes of event for the DI group (26/35, 74.3%) were chest-crushing while the rest were from CPR (9/35, 25.7%). For the VI group, the majority was owing to motorcycle accidents (57/68, 83.8%) followed by car accidents as equal as pedestrian injuries (4/68, 5.9% each), and falls-from-height (3/68, 4.4%). Locations of pulmonary contusion as well as associated injuries of the chest found in both groups were shown in Table 1. Location correspondence between rib fractures and pulmonary contusions in the DI group were presented in Table 2 by the concordance scores as abovementioned, and the comparison analysis showed no statistical significance ($p = 0.09$).

By comparing among different age ranges and BMIs, there was no statistical significance for presence of external wounds and intrathoracic injuries in either DI or VI. Presence of external wound was found to be statistical significance ($p = 0.02$) among different AIS scores only in DI while intrathoracic injuries revealed statistical significance ($p < 0.01$ for cardiac and aortic injuries) in both groups.

Comparison of locations of pulmonary contusion between DI and VI, lesions at hilum of lungs shows significant difference ($p < 0.01$) that those found in VI showed a higher prevalence than those in DI (55.9 against 20.0%). This was similar for intrathoracic injuries and external wounds ($p < 0.01$ and $p = 0.04$, respectively).

Generalized extension of pulmonary contusion was defined by the contusion harboring anterior and posterior of the lung and was observed whether it occurred unilaterally or

bilaterally. Then they were compared among different severities of chest injury assigned be AIS-BR3 in DI and VI. The results were presented in Table 4. Statistical difference was found among different AIS-BR3 in both groups ($p < 0.01$).

Table 1 Demographic distribution, severity score, and intrathoracic associated injury of population for gross pathological study

		DI	VI
Total (n)		35	68
Sex			
	male	26 (74.3%)	59 (86.8%)
	female	9 (25.7%)	9 (13.2%)
Age (yr.)			
	≤20	0	11 (16.2%)
	>20-30	12 (34.3%)	39 (57.4%)
	>30-40	6 (17.1%)	12 (17.6%)
	>40-50	4 (11.4%)	3 (4.4%)
	>50-60	5 (14.3%)	2 (2.9%)
	>60	8 (22.9%)	1 (1.5%)
BMI			
	<18.5	4 (11.4%)	9 (13.2%)
	18.5-22.9	13 (37.1%)	30 (44.1%)
	23.0-24.9	6 (17.1%)	7 (10.3%)
	25.0-29.9	8 (22.9%)	16 (23.5%)
	>30	4 (11.4%)	6 (8.8%)
AIS-BR3			
	3	11 (31.4%)	37 (54.4%)
	4	2 (5.7%)	20 (29.4%)
	5	20 (57.1%)	11 (16.2%)
	6	2 (5.7%)	0
Location of pulmonary contusion			
	hilum only	3 (8.6%)	5 (7.4%)

hilum and other area	4 (11.4%)	33 (48.5%)
anterior or posterior surface	8 (22.9%)	28 (41.2%)
anterior and posterior surfaces	24 (68.6%)	35 (51.5%)
Associated injuries		
External wound	25 (71.4%)	34 (50.0%)
Rib fracture	31 (88.6%)	NA
Tear of bronchial tree	12 (34.3%)	0
Cardiac contusion	5 (14.3%)	7 (10.3%)
Cardiac laceration	16 (45.7%)	4 (5.9%)
Aortic laceration	12 (34.3%)	6 (8.8%)
ascending	7 (20.0%)	0
arch	3 (8.6%)	1 (1.5%)
descending	2 (5.7%)	5 (7.4%)

NA = data not available

Table 2 Location correspondence between rib fracture and pulmonary contusion in DI

Concordance score	AIS-BR 3			
	3 (n = 8)	4 (n = 2)	5 (n = 19)	6 (n = 2)
0	2 (25.0%)	1 (50.0%)	0	0
1	0	0	3 (15.8%)	1 (50.0%)
2	2 (25.0%)	1 (50.0%)	7 (36.8%)	1 (50.0%)
3	4 (50.0%)	0	9 (47.4%)	0

Table 3 Demographic distribution, severity score, and cause of event of population for histopathological study

	n
Total	62
Sex	
male	54 (87.1%)
female	8 (12.9%)
Age (yr.)	
≤20	6 (9.7%)
>20-30	24 (38.8%)
>30-40	10 (16.1%)
>40-50	7 (11.3%)
>50-60	6 (9.7%)
>60	9 (14.5%)
PTI (hr.)	
1-6	28 (45.2%)
>6-12	9 (14.5%)
>12-24	9 (14.5%)
>24-72	5 (8.1%)
>72-168	8 (12.9%)
>168	3 (4.8%)
AIS-BR3	

	3	22 (35.5%)
	4	35 (56.5%)
	5	5 (8.1%)
	6	0
Cause		
	traffic	56 (90.3%)
	fall	4 (6.5%)
	others	2 (3.2%)

Table 4. Extension of pulmonary contusion in association with AIS-BR3

Mechanism	Extension	AIS-BR 3			
		3	**4**	**5**	**6**
DI		n = 11	n = 2	n = 20	n = 2
	not generalized	3 (27.3%)	0	0	0
	unilateral	7 (63.6%)	0	1 (5.0%)	0
	bilateral	1 (9.1%)	2 (100.0%)	19 (95.0%)	2 (100.0%)
VI		n = 38	n = 20	n = 11	n = 0
	not generalized	5 (13.2%)	0	0	-
	unilateral	21 (55.3%)	1 (5.0%)	6 (54.5%)	-
	bilateral	11 (28.9%)	19 (95.0%)	5 (45.5%)	-

Histopathological study

Of the total of 2,012 autopsy cases, there were 271 cases containing pulmonary contusions. However, only 62 survived from 1 to over 168 hours. Distribution of sex, age, AIS-BR3, and causes of event were presented in Table 3. Histopathological sequence was observed for presence of neutrophils, eosinophils, macrophages, lymphocytes, megakaryocytes, and fibroblasts as well as alveolar epithelial necrosis, thrombus, proliferation of type-2 pneumocyte, formation of hyaline membrane, and organizing pneumonia in each PTI subgroups as shown in Table 5 and Figure 1. Chronological changes of histopathology are summarized in Figure 2. In the >168-hr group, there were 2 cases who survived for 16 days and only one who died at Day 30.

Table 5. Histological findings in each PTI

PTI (hr)	Total	n (%)											
		H	Macro	Neutro	Ep nec	Eo	Lymph	Fibro	Mega	Throm	Type-2	Hyaline	OP
1-6	28	28 (100%)	10 (36%)	3 (11%)	2 (7%)	1 (4%)	1 (4%)	1 (4%)	0	0	0	0	0
>6-12	9	9 (100%)	6 (67%)	5 (55%)	3 (33%)	1 (11%)	1 (11%)	1 (11%)	1 (11%)	3 (33%)	0	0	0
>12-24	9	9 (100%)	6 (67%)	6 (67%)	2 (22%)	2 (22%)	1 (11%)	2 (22%)	3 (33%)	2 (22%)	0	0	0
>24-72	5	5 (100%)	5 (100%)	4 (80%)	1 (20%)	2 (40%)	2 (40%)	2 (40%)	1 (20%)	4 (80%)	1 (20%)	0	0
>72-168	8	7 (88%)	7 (88%)	8 (100%)	4 (50%)	7 (88%)	8 (100%)	4 (50%)	7 (88%)	5 (63%)	2 (25%)	1 (13%)	1 (13%)
>168	3	3 (100%)	1 (33%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	0	2 (66%)	3 (100%)	3 (100%)

H = hemorrhage, Macro = macrophage, Neutro = neutrophil, Ep nec = alveolar epithelial necrosis, Lymph = lymphocyte, Fibro = fibroblast, Mega = megakaryocyte, Throm = thrombus, Type-2 = type-2 pneumocyte, Hyaline = hyaline membrane, OP = organizing pneumonia

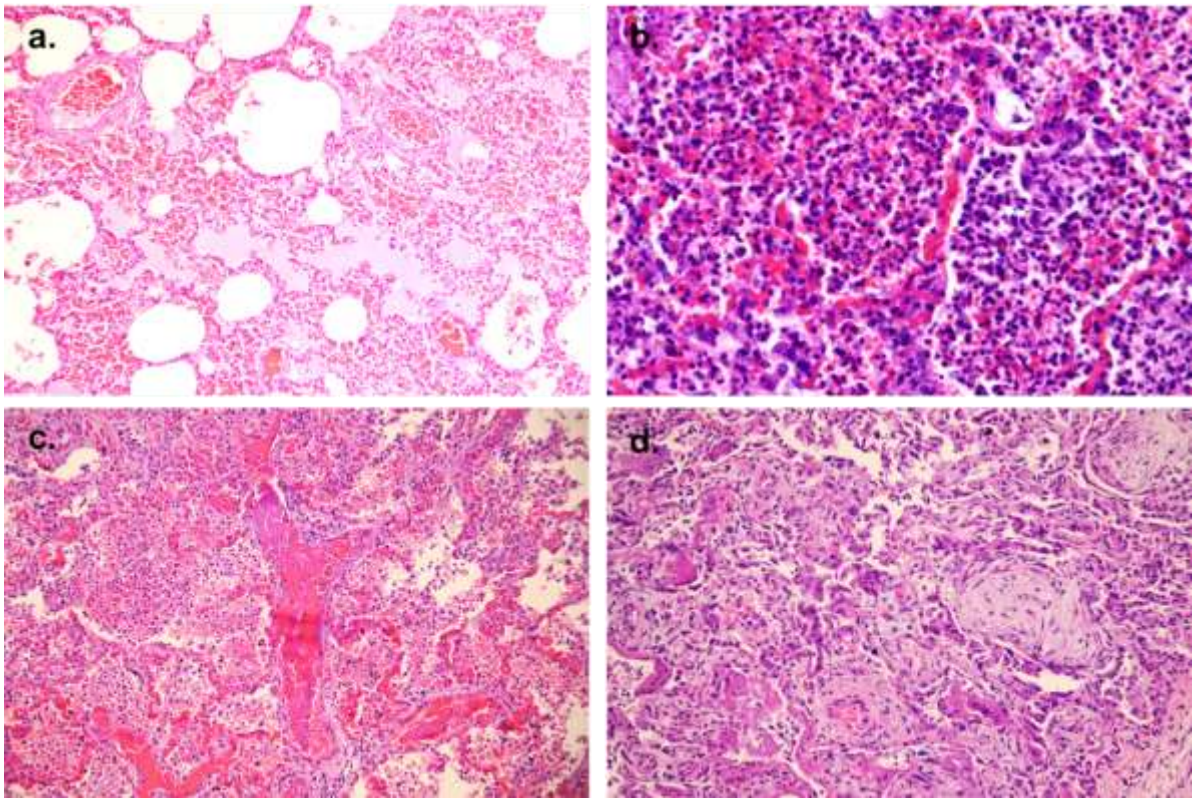

Figure 1: H&E-stained slides of pulmonary contusions show histopathological sequence.
a. alveolar hemorrhage is a main characteristic of pulmonary contusion until 3-hr PTI, few neutrophils per alveolus are detected. b. neutrophils becomes predominant in alveoli Day 3. c. Day 7 PTI, eosinophils and lymphocytes are obviously seen as well as hyaline membranes and thrombi. d. Day 16 PTI, organizing pneumonia develops in the second week and occupies almost alveolar spaces at Day 30.

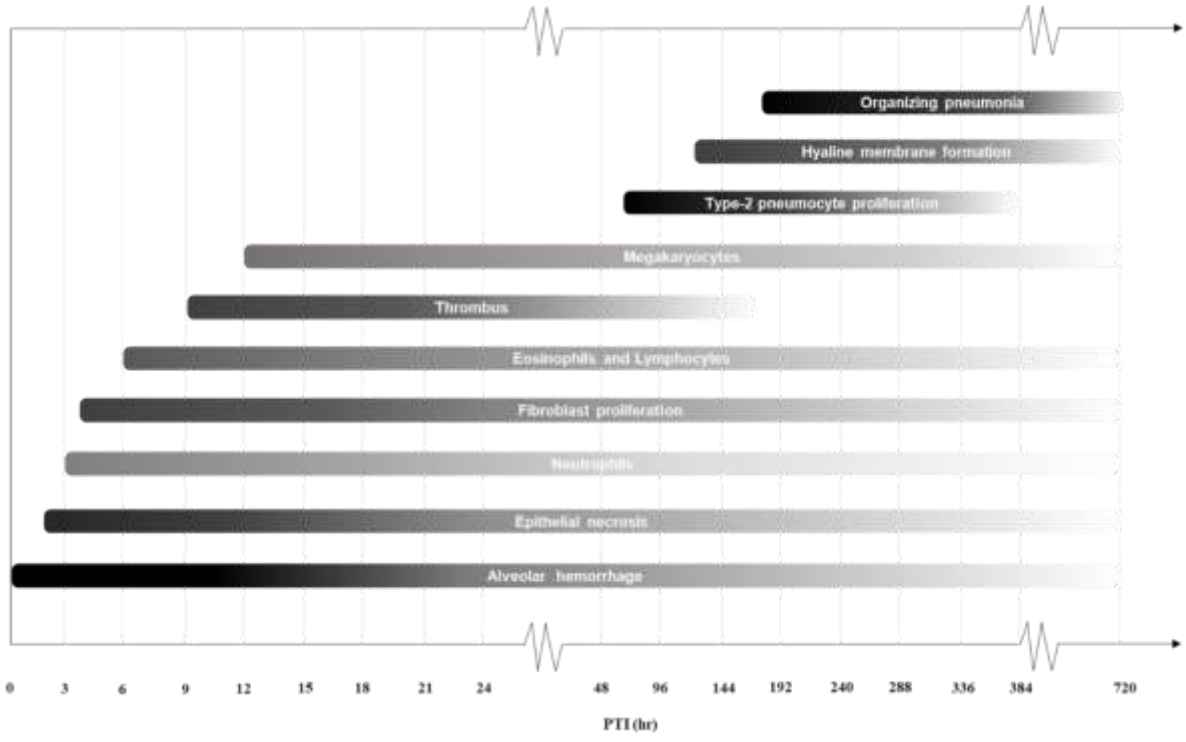

Figure 2. Summary of histopathological sequence in pulmonary contusion

Discussion

To date, pulmonary contusion is accounted for 25-35% of blunt chest trauma [11]. Clinical hypoxemia and hypercapnia have been reported to reach the peak in the first 72 hours after injury [4]. Severe pulmonary contusion can cause deterioration of clinical outcomes that potentially leads to ARDS [1] and high mortality of approximately 10-20% [12]. To distinguish between two mechanisms of injury-DI and VI-several characteristics of gross pathology should be accumulated to make more precise inference that is substantial in forensic practice.

Forensic aspects of gross pathology

Mechanisms of pulmonary contusion have been summarized into three possible ways which are inertial effect, spalling effect, and implosion effect [4-6]. The first mechanism is resulted from a shearing movement between hilar and peripheral areas that is accounted for VI [4]. No matter what mechanism causing lungs to impact chest wall, the second mechanism is owing to a rupture of alveolar wall from the direct impact either by crushing or acceleration-deceleration [4]. The third mechanism is mainly found in blast injuries because shock wave initiates air in alveolar spaces to explode [6,13]. From these three propositions, pulmonary contusions should have been principally generated by the spalling effect. One of the supporting reasons from this study is that pulmonary contusions are not necessarily associated with rib fractures clearly seen in the DI group. It may occur solely at any location where applied pressure high enough to injure an alveolar wall. Another biomechanical model that has been widely studied in car crashes is called Viscous Criterion (VC) [14]. The VC is derived from the maximum product of velocity of deformation and normalized chest compression that the chest wall is largely bent during impact causing crushing forces to intrathoracic viscera [14-15]. The VC could be analogous to the situation similar to car crashes for correlating the overall risk of visceral and soft tissue injuries [16].

Severity of pulmonary contusion tends to increase with respect to AIS-BR3. Bilateral generalized lung contusions are more common from the AIS-BR3 score 4 onwards as similar to the previous report [1]. In clinical settings, severities of pulmonary contusion are associated with increases in hospitalization and intubation duration [17]. It could increase mortality when there are a greater number of associated injuries [6]. In case that patients with less severe pulmonary contusions survive for a reasonable period of time, it will resolve within 3 to 14 days [18].

To find different characteristics between DI and VI, the results show significant difference of pulmonary contusions at hilar areas that those in the VI group are of a higher prevalence than those in the DI group. This may be consistent with the inertial effect because acceleration-deceleration plays a more important role for VI than DI. On the opposite side,

associated injuries of chest including presence of external wounds, injuries of bronchial tree, cardiac injuries, and aortic injuries are of higher prevalence in DI than VI with statistical difference.

Unsurprisingly, external wounds of the chest as well as injuries of the heart, bronchial-tree, ascending, and arch of aorta could be explained by crushing of the chest wall that results in either direct pressure applied to the chest wall and intrathoracic viscera or increased intrathoracic pressure causing overstressing of cardiac chambers as proposed in the previous studies [19-21]. However, laceration of descending aorta in VI shows slightly higher prevalence than DI similar to the prior study [22]. This could be owing to a sudden deceleration commonly occurs at the isthmus [23]. To summarize, contusions of the lung hila in association with injuries of descending aorta especially at the isthmus could be good characteristics to infer that the mechanism may be VI rather than DI.

Histopathological sequence

The initial pathology of lung contusion in animal models begins with alveolar hemorrhage, edema, and sometimes collapse [24]. This is comparable to the findings in the actual human histopathology in this study. It is initiated by loss of alveolar membrane-capillary integrity [25] leading to increase vascular permeability and pulmonary edema [24]. As found in this study, neutrophils then migrate into alveolar spaces after a few hours PTI and they, in conjunction with degranulated alveolar macrophages, are believed to release several chemokines, for example, C3a, IL-1β, IL-6, IL-8, and KC to attenuate increased vascular permeability [24-26]. Therefore, edematous fluid reduces lung surfactant and, as in animal models, forming the early phase of ARDS by 5 to 14 PTI [24,26]. This study also find that neutrophils continue to migrate and predominantly occupy injured alveolar spaces in 3 days PTI similar to what has been found in animal models [27].

Roles of eosinophils which are found to appear after 6 hours PTI in this study, are found in the animal model that they may be induced by some cytokines such as IL-33 from airway epithelia to counter regulate inflammation and might play protective roles in many aspects such as protection against some types of bacterial pneumonia [28]. However, their actual mechanisms are not yet thoroughly understood.

We also detect thrombus in small branches of pulmonary artery after 9 hours PTI. Though it is so-far unclear how this occurs, it resembles to what has been reported of de novo pulmonary thrombosis without DVT in the murine experiment [29]. To our observation, thrombosis presents until 7 days PTI.

Interestingly, detection of megakaryocyte just a few hours after presence of thrombus throughout the maximum survival time in this study may indicate roles of megakaryocyte not only promoting blood coagulation but also involving in an immune response and inflammation

in pulmonary diseases [30-31]. Lung-resident megakaryocytes (MkL) have been discovered to secrete various cytokines to promote fetal lung development [30]. Driven by tissue-immune environment such as IL-33, MkLs play key immune regulatory roles in vivo and in vitro such as to protect against bacterial pathogens [32]. They have been detected in pulmonary pathology from COVID-19 and ARDS [31].

After 3 to 5 days most of pulmonary contusions resolve [6,26], however some individuals may develop ARDS. Type-II pneumocytes (AT2) is believed to involve in stabilizing host immune-competence and is potentially substantial resources for lung regeneration and repair [33]. We observe proliferation of AT2 from a few days PTI. The underlying process is thought to be promoted by the Jagged-1/Notch signaling pathway [34]. However, as a result of inflammatory pathways as well as intra-alveolar hemorrhage that promotes bacterial pneumonia [6] as well as predisposing clinical factors such as sepsis and multiple transfusions, these tie to the highest incidence of ARDS that leads to mortality rates of approximately 29-42%[25]. The data in our study show that hyaline membrane can be seen at the end of the first week PTI, and organizing pneumonia develop after the first week as a pathology of ARDS.

Conclusion

We find that DI harbors statistical significance of some gross findings of pulmonary contusion as well as of other associated intrathoracic injuries to distinguish from VI. Also, the histopathological sequence ranging from 1 hour to 30 days PTI show interesting findings that can be linked to the previous studies in animals. This could be useful to help infer mechanisms of injury from gross pathology as well as dating the PTI from histopathology.

Acknowledgement

Not applicable

References

(1.) Mahmood I, El-Menyar A, Younis B, et al. Clinical significance and prognostic implications of quantifying pulmonary contusion volume in patients with blunt chest trauma. Med Sci Monit. 2017; 23: 3641 - 8.

(2.) Weaver AA, Danelson KA, Armstrong EG, et al. Investigation of pulmonary contusion extent and its correlation to crash, occupant, and injury characteristics in motor vehicle crashes. Accid Anal Prev. 2013; 50: 223 - 33.

(3.) Rendeki S, Molnár TF. Pulmonary contusion. J Thorac Dis. 2019; 11(Suppl 2): S141 - 51.

(4.) Cohn SM, Dubose JJ. Pulmonary contusion: an update on recent advances in clinical management. World J Surg. 2010 Aug; 34: 1959 - 70.

(5.) Clemedson CJ. Blast injury. Physiol Rev. 1956; 36: 336 - 54.

(6.) Ganie FA, Lone H, Lone GN, et al. Lung Contusion: A clinico-pathological entity with unpredictable clinical course. Bull Emerg Trauma. 2013; 1: 7 - 16.
(7.) O'Connor JV, Kufera JA, Kerns TJ, et al. Crash and occupant predictors of pulmonary contusion. J Trauma. 2009; 66: 1091 - 5.
(8.) WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004 Jan 10; 363(9403): 157 - 63. doi: 10.1016/S0140-6736(03)15268-3.
(9.) Gennarelli TA, Wodzin E. Abbreviated injury scale 2005: update 2008. Barrington, IL: Association for the Advancement of Automotive Medicine; 2008.
(10.) Sayeed RA, Darling GE. Surface anatomy and surface landmarks for thoracic surgery. Thorac Surg Clin. 2007; 17: 449 - 61.
(11.) Moloney JT, Fowler SJ, Chang W. Anesthetic management of thoracic trauma. Curr Opin Anaesthesiol. 2008; 21: 41 – 6.
(12.) Danelson KA, Chiles C, Thompson AB, et al. Correlating the extent of pulmonary contusion to vehicle crash parameters in near-side impacts. Ann Adv Automot Med. 2011; 55: 217 - 30.
(13.) Bridges EJ. Blast injuries: From triage to critical care. Crit Care Nurs Clin North Am. 2006; 18: 333 – 48.
(14.) Viano DC, Lau IV. A viscous tolerance criterion for soft tissue injury assessment. J Biomechanics. 1988; 21: 387 - 99.
(15.) Viano DC, Lau IV, Asbury C, et al. Biomechanics of the human chest, abdomen, and pelvis in lateral impact. Accid Anal Prev. 1989; 21: 553 - 74.
(16.) Cui J, Rapo M, Mathews K, et al. Biomechanically based correlate for localized lung contusion from nonlethal blunt impact projectiles. Mil Med. 2021; 186(Suppl 1) :331 - 8.
(17.) Zingg SW, Millar DA, Goodman MD, et al. The Association between pulmonary contusion severity and respiratory failure. Respir Care. 2021; 66: 1665 - 72.
(18.) Wanek S, Mayberry JC. Blunt thoracic trauma: Flail chest, pulmonary contusion, and blast injury. Crit Care Clin. 2004; 20: 71 – 81.
(19.) Kaye P, O'Sullivan Í. Myocardial contusion: emergency investigation and diagnosis. Emerg Med J. 2002; 19: 8 - 10.
(20.) Kirsh MM, Orringer MB, Behrendt DM, et al. Management of tracheobronchial disruption secondary to nonpenetrating trauma. Ann Thorac Surg. 1976; 22: 93 – 101.
(21.) Altinok T, Can A. Management of tracheobronchial injuries. Eurasian J Med. 2014; 46: 209 - 15.
(22.) Pelletti G, Cecchetto G, Viero A, et al. Traumatic fatal aortic rupture in motorcycle drivers. Forensic Sci Int. 2017; 281: 121 - 6.
(23.) Butler KL, Moore EE, Harken AH. Traumatic rupture of the descending thoracic aorta. AORN J. 1996; 63: 917 - 25.

(24.) Hellinger A, Konerding MA, Malkusch W, et al. Does lung contusion affect both the traumatized and the noninjured lung parenchyma? A morphological and morphometric study in the pig. J Trauma. 1995; 39: 712 - 9.
(25.) Johnson ER, Matthay MA. Acute lung injury: epidemiology, pathogenesis, and treatment. J Aerosol Med Pulm Drug Deliv. 2010; 23: 243 - 52.
(26.) Machado-Aranda D, V Suresh M, Yu B, et al. Alveolar macrophage depletion increases the severity of acute inflammation following nonlethal unilateral lung contusion in mice. J Trauma Acute Care Surg. 2014; 76: 982 - 90.
(27.) Raghavendran K, Davidson BA, Woytash JA, et al. The evolution of isolated bilateral lung contusion from blunt chest trauma in rats: cellular and cytokine responses. Shock. 2005; 24: 132 - 8.
(28.) Krishack PA, Hollinger MK, Kuzel TG, et al. IL-33-mediated eosinophilia protects against acute lung injury. Am J Respir Cell Mol Biol. 2021; 64: 569 - 78.
(29.) Brown IE, Rigor RR, Schutzman LM, et al. Pulmonary arterial thrombosis in a murine model of blunt thoracic trauma. Shock. 2018; 50: 696 - 705.
(30.) Yeung AK, Villacorta-Martin C, Hon S, et al. Lung megakaryocytes display distinct transcriptional and phenotypic properties. Blood Adv. 2020; 4: 6204 - 17.
(31.) Huang DY, Wang GM, Ke ZR, et al. Megakaryocytes in pulmonary diseases. Life Sci. 2022 Jul 15:301:120602. doi: 10.1016/j.lfs.2022.120602.
(32.) Pariser DN, Hilt ZT, Ture SK, et al. Lung megakaryocytes are immune modulatory cells. J Clin Invest. 2021 Jan 4;131(1): e137377. doi: 10.1172/JCI137377.
(33.) Olajuyin AM, Zhang X, Ji HL. Alveolar type 2 progenitor cells for lung injury repair. Cell Death Discovery (2019) 5:63 https://doi.org/10.1038/s41420-019-0147-9.
(34.) Zembacher R, Desole S, Linhart C, et al. Proliferation of alveolar type II pneumocytes is stimulated by Jagged-1 in vitro. Eur Respir J. 2012; 40(Suppl 56): P3759.

REVIEW ARTICLE

THE LAWS OF THE CAUSE OF DEATH AND THE ROLE OF THE AUTOPSY: REMINISCENCES OF

THE ANATOMICAL PATHOLOGIST AND MEDICOLEGAL INVESTIGATOR OF DEATH

Akinwumi Oluwole KOMOLAFE

Department of Morbid Anatomy and Forensic Medicine,
Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria.
Email: akinkomo1@yahoo.com
Mobile Phone number: +234 8033557741

Submitted: *30 March 2023*
Accepted: *9 April 2023*
Published: *1 December 2024*

Abstract

Death though the final end of all men remains a humbling experience that throws off diverse challenges. These include questions about the manner, mechanisms and cause of death. Thereafter, a death certificate will be issued highlighting the relevant biodata of the deceased and more importantly the causes of death in their evolutionary pattern. The sensitive nature of the fall-outs of death demands that the facts be assayed with diligence. The autopsy is the unassailable gold standard investigation to unravel antemortem events with utmost certainty. The autopsy as an auditor of the processes that led to death cannot be left at sea. Relevant laws ought to be in place that guide the evaluation of the process of death with a systematic approach, using logical assessment of the knowledge of pathogenesis, pathophysiology and the outcome of diseases without undue extrapolations. Formulating rational laws to determine issues related to death postmortem is crucial to setting records straight and avoiding ambiguities that may further evoke medicolegal dilemmas.

Keywords: Laws, cause of death, medicolegal investigation, diseases, autopsies, death certification.

Introduction

Death is an inevitable end of every mortal. Death may be a consequence of acute sickness, chronic diseases, terminal diseases and longstanding pathological conditions[1]. Death is not always an absolute end in itself as it may evoke the opening of a new chapter of diverse questions bordering on ethical issues, medical negligence and malpractice, professional discipline and legal challenges, which may include gross negligence manslaughter[2–6]. Such questions include the identity of the deceased, the circumstances and mechanisms of death, the cause of death among many other pertinent issues, succinctly captured by the Komolafe's '12Cs' of relevant questions in medicolegal autopsies[7]. Death evokes the writing by the physician or procurement by relatives of a death certificate (DC), a permanent medical and

legal record of an individual's death[8]. The DC is an important medico-legal document for the managing physician and deceased's relatives who desire to claim inheritance and insurance policies and for recognizing inheritable genetic diseases or identifying risk factors for potentially communicable diseases[8–10]. Proper certification of death and understanding of death mechanisms through appropriate medicolegal death investigation is also a vital data collection means for epidemiological studies that could boost health care delivery[8-9,11-12]. Establishing the cause of death may be difficult as the circumstances surrounding death may not be explicit, especially in suspected homicides or atypical presentations or disease with rapidly evolving pathogenesis with unwholesome pathophysiological progression and fatal consequences the consequence of this is that the medical certificate of the cause of death continues to be is one of the most inaccurately completed documents[9,11,13-14] It must be emphasized that it is the physician's responsibility to certify a patient dead and complete the medical part of the death certificate, having thoroughly scrutinised every available document, result of investigations with regards to the patient[9] However, although the guidelines on death certification are widely available, they are rarely used in many countries[9]. When the physician is unable to write a correct death certificate, it behoves him to act in the best ethical, professional and public interest to ask for an autopsy and use the information derived from the autopsy, a gold standard in cause of death evaluation to write a death certificate[15] The postmortem examination then becomes necessary to unravel the cause of death[16–18] The proper interpretation of the morphological findings is crucial to making the best judgement on the causes and circumstances of death[19-20]. This becomes highly imperative, considering that medical records, particularly death certificates may undergo legal scrutiny to evaluate the appropriateness of the cause of death in individual patients, particularly if there are postmortem related issues involving inheritance issues, antemortem life/health insurance by the deceased and appropriation of the estate of the deceased.[11] The potential developments after demise and the ripple effects should make the stakeholders in death management to explore all possible mechanisms to ensure the best documentations are made with regards to the circumstances of death. The postmortem examination as a seemingly unassailable mechanism to establish the truth or facts about the deceased, demands moral commitment to be carefully performed, diligent observation, thorough exercise of the knowledge pathogenesis and pathophysiology and systematic interpretation needs to be carefully performed and interpreted within the overall circumstances of the patient[21].

The autopsy, though a time-honoured gold standard procedure in investigating issues relating to death and corelating with antemortem events is not entirely devoid of errors of judgement, interpretation and conclusion, sometimes through innocent subjective long-held inclinations[19,22]. Komolafe decried the subjective interpretation of the autopsy as it does not give high credence to set standards and guidelines[20]. To avoid the besetting nature of human fallibility due to inexperience, exaggerated sense of understanding, unduly extrapolated

knowledge and peculiar individual idiosyncrasies, it then becomes important to set laws and principles that help the anatomical and forensic pathologist to properly conclude on issues related to death without bias[23].

A stepwise approach to establish the cause of death through pertinent questions

The prime place of the proper formulation of the cause of death cannot be overemphasized. The cause of death is the injury or disease that produces the sequence of events with ensuing physiological derangement in the body, resulting in death[24]. The cause of death has two components, the primary and secondary causes of death[24-25]. The primary cause of death includes the immediate and antecedent/intermediate causes responsible for the fatal outcome, while the secondary cause of death includes the conditions that are not related to the primary cause of death but contribute substantially to the death of an individual, not incidental findings[24]

The determination of the cause of death and the documentation on the death certificate is crucial for structured implementation of health policies by health decision makers and planners through the extensive use of mortality statistics, the quality of which depends on the processes that generate the death certificates[9-10].

Establishing the cause of death is very important for so many reasons. It obviates highly consequential errors that compromise statistical data, which could mislead health policy planners and epidemiologists as well as hinder the processing of insurance claims[10,26]. Thus, the autopsy also has immense public health and by implication social benefits[27–29]. The pertinent question is how may we approach difficult autopsy cases in order to endure the best outcomes regarding the cause of death?

The most questions would include:

What is the organ of interest considering the clinical features, past medical history and the events preceding death terminally? This will require careful examination and diligent analysis of every bit of clinical history and result of investigations.

What are the morphological findings, well characterized into morphologies of primary disease, predisposing factors, complications of the disease process et ce te ra?[30]

Which lesions best reflect the primary or underlying disease that initiated the sequence of events that culminated in the death of the patient?[31-32]

What were the intermediate and terminal events that resulted in death?

What ae the applicable laws, principle and guidelines of autopsy interpretation in the index case?[20]

Furthermore, the following questions as indicated by Komolafe are crucial to resolving dilemmas at autopsy sessions and remain quite germane in defining the underlying disease/cause, antecedent/intermediate and immediate causes of death:[31]

a. Determining the structural alterations or lesions in the organs: What are the major and perhaps minor structural alterations observed during autopsies in individual tissues and organs of the body, diligently interpreted in an overall sense, with the background knowledge of pathogenesis, structural and functional relationships between organs? The overall attribute of a lesion ultimately defines the nature and of course the disease process. Thus, lesional morphology is a complete appraisal of its identities: the morphology (the study of appearances in this case the structure in all entirety? shape, colour, size (in three dimensions and weight), consistency, secondary changes such as cystic degeneration, haemorrhages etc?
b. Defining the pattern of the lesions and the diseases known to cause those lesions: What diseases known in literature as reported in case series have been proven to impact those lesions and what exactly is the evolutionary pattern of the lesions? This will guide the pathogenesis and pathophysiology.
c. Deciding whether the lesions have a bearing on one another, perhaps consequences of altered relationships, especially in organs with complementary functions.
d. Determining what disease triggered off the sequence of events leading to the pathologies: Can a single disease process explain the different lesions or are the lesions expressions of the anatomic components of a syndrome?
e. Deciding on the evolutionary pattern based on pathogenesis: What are the evolutionary trends of the lesions in the index patient?
f. Determining the correlation between the morphology and clinical features: How has the pathological events created abnormal functioning with resultant clinical features in the patient? This is essentially clinicopathological correlation from a background knowledge of functional significance or clinical correlation.
g. Deciding on the most probable lesion through critical evaluation of available morphological evidence even though there are exuberant differential diagnoses capable of causing conflicts: How strong are some possibilities compared to others due to available morphological evidence, strengthened by differential diagnoses?
h. Determining the stage of the disease process by critically evaluating the sequence of lesions in order to decide the contributions of the lesions to death and the extent of the disease as at the time of death.
i. Determining the modifiers and modulators of the disease process: The application of the knowledge of factors that could alter known pathogeneses and pathophysiology is crucial to unbiased determination of the cause of death. Circumstances and interplay of forces may modify or modulate the disease process. These include iatrogenic interventions, drugs, idiosyncratic reactions, environmental factors, morbidities, syndromic associations, synchronous, metachronous and collision tumours.

j. Determination of the categories of the complications: The ability to classify the morphologies appropriately is important in avoiding misinterpretations and missing out on the exact cause of death. Morphologies of the complications of the disease condition must be clearly delineated from the complications of the treatment or procedures with iatrogenic impartations, which may have medicolegal implications. It is very important to know if there were any medical interventions that resulted in death and how significant were such interventions in initiating the process of death, especially when related to surgical procedures?

k. Determining the exact cause of death within the true circumstances of the events leading to death consummates the autopsy session: This involves summating the evidence by possibilities, arranging differential diagnoses in order of clinicopathological significance and importance and distinguishing between the proximate, intermediate and the immediate causes of death. Chance morphologies that are not contributory to the disease process are incidental findings and are not part of the cause of death and are not indicated in the death certificate.

The Laws of the Cause of Death

1. **The inevitable end law:** Death is an inevitable end, the final event of every mortal which has an anatomopathological relationship in terms of cause and effect, including organ structural depreciation and functional declination due to old age[33]. *The law states that "death is a most certain end of all mortals, either caused by a progressive age-related degeneration of anatomical structure with ultimately fatal physiological compromise or organic disease which ultimately causes death through worsening physiological dysfunction of a major organ or multiple organ failure".*
2. **The ultimate consequence of terminal disease law:** Terminal diseases or malignancies will ultimately result in death.[34] *The law states that "cancers and malignancies are terminal diseases capable of causing death by chronic structural damage through local invasion or metastasis to invalidate tissue integrity or by acute phenomena such as spontaneous haemorrhage or iatrogenic death acceleration associated with hazards of investigation to diagnose, monitor therapy or complications of therapy including patient related factors."*
3. **The anatomo-physiological dissociation law:** Diseases are multistage problems, are products of anatomo-physiological perversions and could only cause death if significant physiological dysfunctions dovetail anatomical structural compromise. Otherwise, the pathologist should find another explanation for the death. *The law states that "all manners of diseases even when potentially treatable may invariably progress from one stage to another until the terminal stage or irreversible complication sets in to cause death".*

4. **Cause and effect cum progression law:** Death always has an initiating event/proximate disease, a significant intermediate event and a consequential terminal event that culminates in death.[23,35] *The law states that "the organic basis of disease is incontrovertible but do not cause death in isolation but go through progressive further decelerations until a structural anatomical event correlates with and culminates in a fatal physiological outcome."*
5. **The acute injury, assault or compromise law:** Sudden deceleration of function of an organ may occur if there is an acute insult or injury that compromises the borderline physiology or adjusted state. *The law states that "an acute exacerbation of a chronic debilitating illness could result in death in the absence of appropriate medical intervention to prevent worsening compromised physiology."*
6. **The chronic disease neglect law:** A chronic disease without medical intervention may progress faster than if appropriate medical intervention retards its progression until crucial anatomical structures vital to survival through physiological regulators are lost or fail, affect other dependent structures and death occurs. *The law states that "in the absence of appropriate medical interventions to treat or retard the progression of a chronic disorder, progressive anatomical distortions, disruptions and effacements will ultimately end in correlatory fatal physiological events".*
7. **The iatrogenic damage law:** Death could inevitably result from deliberate or non-deliberate iatrogenic interventions. Such interventions may be ill-advised, contraindicated, presumptuous or a product of lack of training or product of medical error of judgement or practice. *The law states that "deaths can occur from iatrogenic interventions whatever the motive or bases if anatomical structures undergo significant gross or microscopical damage with fatal physiological correlates".*
8. **The acute hazard deceleration law:** Death could be the end result of an acute episode such as accident (road, air or drowning on boat/ferry ride) or severe anatomical compromise such as a dissecting aneurysm causing pericardial collection resulting in cardiac tamponade and cardiogenic shock. *The law states that "an acute hazardous event in spite of supposedly perfect homeostatic conditions could quickly result in death."*
9. **The interdependent law:** Any disease, acute or chronic which significantly alters or obliterates the structure of an organ such that it significantly compromises its basic regulatory function to sustain and enable life or incapacitates its anatomic dependants, would eventually result in death. *The law states that "anatomically and physiologically interdependent organs would suffer congruous decline till their functions and ability to sustain life is lost and death occurs."*
10. **The systematic progression law:** The certificate of death reflects its evolution from initiating cause to intermediate and immediate causes. The death certificate is essentially a systematic recapitulation of the pathogenesis of the disease processes and

pathophysiological phenomenon and stagewise progression until events culminate in death. The law states that *"in the certification of the cause of death, death is not absolutely caused by an event without intervening events and a consequence of final event which is the immediate cause of death"*

11. **The law of exclusion of incidental findings:** Deaths are not caused contextually by incidental morphologies, which if indeed they are significantly implicated in process of death are not classifiable as incidental findings. Incidental findings are chance findings during postmortem examination without any contributions to the process of death.[33] *The law states that "the cause of death must be explored when a morphological finding or disease condition that contributes to death by any means is still regarded as an incidental finding".*
12. **The probability law:** In sudden deaths or sudden unexpected deaths, in which natural causes are presumed to be the causes of death, the pronouncement of the initiating cause with absolute certainty should only be done when there is very high probability at the stage of death and anatomic compromises sufficiently dovetails the pathophysiological dysfunction to result in death when all other possible differentials have been ruled out and possibly toxicology has been done and interpreted within the context of the overall circumstances of the deceased. *The law states that "the degree of certainty of the cause of death in any case is directly proportional to its incompatibility with life, the pathophysiologic correlate to incapacitate the ability to sustain the basic functions of life."*

In establishing the exact cause of death in sudden natural deaths, careful scrutiny of the processes leading to death is crucial to finding the true cause of death[(36)]. This is exemplified by Kemp and Barnard who classified the causes of death into five definite groups[(37)]. While class 1 category accounts for approximately 5% of natural deaths in the medicolegal population, including examples such as ruptured myocardial infarcts, ruptured dissecting aortic aneurysms, rapidly evolved moderate to massive intracerebral haemorrhages; class 2 category accounts for 90% of cases of natural deaths in the medicolegal population with examples cases being diseases that have the potential of considerable chronicity especially if factors favour it. Such cases include advanced heart diseases, chronic lung diseases, advanced or metastatic malignancies and complications of chronic alcoholism[(37)]. According to Kemp and Barnard, the diseases in class 3 category are infrequent in the medicolegal population, have marginal lethal potential as identified at autopsy, but on their own, they are not sufficiently advanced to be taken to be able to cause death if there are no inputs of other pathological conditions having meticulously reviewed the morphological findings at autopsy which may act in synergy with them to cause death. Therefore, adjudging them as stand-alone cause of death would need the careful consideration of a highly convincing history as well as careful exclusion of other

causes that may possibly explain the fact of death in the index case. In the absence of any other likely causes, the examples of class 3 category cause death would include circumstances such as witnessed collapse in the setting of moderate coronary artery disease at autopsy and negative toxicology with absence of other significant pathological findings. Thorning's study further lays credence to atherosclerosis-related disease, particularly primary coronary disease, as a leading cause of death among men and women with its incidence, prevalence and mortality rate notorious for rising steeply with age and indeed known to double every 5 years after 24 years of age as the disease worsens[29]. In class 4 category, there is a formidable and compelling clinical history of a known disease, which could be potentially lethal but there are no demonstrable lethal structural alterations at autopsy capable of causing and explaining death. Examples of such diseases include epilepsy and asthma. Autopsy is therefore very important in excluding alternative explanations. Kemp and Barnard further opined that in a class 5 category, the cause of death remains undetermined after crime and death scene investigation, full and thorough autopsy with extensive ancillary investigations and meticulously toxicological studies with no available evidence to link death to unnatural causes[37]. Keyvan also emphasizes the rapidly fatal nature of myocardial infarction and cardiac tamponade, especially if they are missed and there was no intervention antemortem[28].

13. **The medical malpractice fall-out law:** In suspected medical negligence and malpractice, health care practitioners' contributions to in death is only plausible if their acts of commission or omission significantly affects the chances of patient's survival or accelerates the process of death[29,38]. This is the basis of the gross negligence manslaughter suits in criminal law[39-40]. *The law states that "an act of clinical negligence or medical malpractice is most certainly a harbinger of death if it inevitably sets off the spiralling events of death when such could not have occurred in the absence of the physician's unwholesome act of commission or omission."*
14. **The biochemical injury or metabolic death law:** Death could result from high levels of exogenous or endogenous toxins, use of drugs contraindicated in cases arising from prescription or inappropriate metabolic fall-outs of pathophysiological events of diseases or by-products of chemical agents[41]. "*The law states that in the presence of fatal levels of a toxic chemical agent with acute or chronic effects capable of shutting down enzyme systems, causing organ failure or causing cardiac arrest, death may be ascribed to biochemical injury in the absence of an overriding anatomic lesion ascribable to a disease process capable of causing death on its own."*
15. **The conjoint effect law:** Multiple pathologies may not individually exhibit high anatomo-pathologic and physiologic correlation to cause death. In such cases, generating the cause of death as being due to the effects of the multiple pathologies is plausible[21]. *"The law states that in the presence of two or more anatomic lesions with none having significant*

deleterious consequence of death on their own, all lesions should be regarded as jointly contributing to death."

16. **The morphologic appraisal law:** The knowledge of disease processes vis a vis pathogenesis, pathophysiology squarely puts the burden of the primary or initiating disease on the lesions that sets off the cascade of events leading to death[33]. *The law states that "the process of death is always initiated by a primary disease with obvious diagnostic criteria and it is solely capable of explaining the subsequent morphological findings of interventions that resulted in death"*

Clinical autopsies or hospital-based autopsies represents the most versatile and all-encompassing opportunity to integrate and correlate the morphological findings of postmortem examination, with antemortem surgical pathology biopsy investigations, other clinical pathology tests with sometimes variable and perplexing clinical features during clinical care[33,42].

The don'ts of medical certification of death

In writing the death certificate, it is very important to avoid all ambiguities that may call the integrity of the document to question[11]. Kotabagi *et al* counsels that terminal events such as circulatory failure, respiratory failure and modes of dying should be avoided in the death certificate as they represent the signs of death without adding value to the information surrounding the circumstances of death with regards to the underlying disease process[33]. Kotabagi further stressed that should they be entered; they must not occur as sole entries but the disease which led to them must be entered in the next line[33]. Kemp and Barnard also stressed that the mechanisms of death such as ventricular fibrillation, respiratory arrest and exsanguination should not be listed on the medical certificate of death[37]. Meyers also affirmed that cardiorespiratory failure being a terminal event in many deaths is non-specific and need not be listed in death certificates[23].

Conclusion

Death though final is not always a predictable event but a careful consideration of all circumstances about the case: the clinical history, the family history, strict appraisal of the morphological findings and explaining them in the light of the knowledge of pathophysiological progression of diseases. The certification of death is a definite event and the document of the medical certificate of the cause of death is a medicolegal document where the precision of the cause of death is indispensable. Any doubt or aspersions of the cause of death written on the death certificate makes the document potentially legally contestable and violable. The anatomical and forensic pathologist investigating the cause of death in diseases should leave no stone unturned but meticulously consider all morphological findings and make the interpretations in the light of classified pathogenesis and pathophysiology of diseases.

References

(1.) Tejerina E, Esteban A, Fernández-Segoviano P, et al. Clinical diagnoses and autopsy findings. *Crit Care Med* 2012; 40: 842 – 6.

(2.) Hodson N. Bawa-Garba ruling is not good news for doctors. *J Med Ethics* 2019; 45: 15 - 16.

(3.) Samanta A, Samanta J. Gross negligence manslaughter and doctors: Ethical concerns following the case of Dr Bawa-Garba. *J Med Ethics* 2019; 45: 10 – 4.

(4.) Ferner RE. Medication errors that have led to manslaughter charges. *Br Med J* 2000; 321: 1212 – 6.

(5.) Komolafe AO, Adefidipe AA, Akinyemi HAM, et al. Medical Errors Detected at the Autopsy: A Prelude to Avoiding Malpractice Litigations. *J Adv Med Med Res* 2018; 27: 1 – 8.

(6.) Beh PSL. Medical manslaughter. *Hong Kong Med J* 2018; 24: 333 – 4.

(7.) Komolafe AO, Akinyemi HAM, Ogunrinde OV, et al. Coroners' Autopsies and Medicolegal Evidence : Have We Always Answered the Crucial Questions ? *Niger J Heal Sci* 2022; 19: 45 – 50.

(8.) Ranson DL, Bugeja L. Medicolegal Death Investigation: Coroner and Forensic Pathology Functions and Processes in Victoria, Australia. *Acad Forensic Pathol* 2017; 7: 567 – 81.

(9.) Maharjan L, Shah A, Shrestha KB, et al. Errors in cause-of-death statement on death certificates in intensive care unit of Kathmandu, Nepal. *BMC Health Serv Res* 2015; 15: 1 – 8.

(10.) McGivern L, Shulman L, Carney JK, et al. Death certification errors and the effect on mortality statistics. *Public Health Rep* 2017; 132: 669 – 75.

(11.) Brooks EG, Reed KD. Principles and pitfalls: A guide to death certification. *Clin Med Res* 2015; 13: 74 – 82.

(12.) Das RK. Medical certification of cause of death. *Medico-Legal Updat* 2009; 9: 28 – 33.

(13.) Nashelsky MB, Lawrence CH. Accuracy of Cause of Death Determination Without Forensic Autopsy Examination. *Am J Forensic Med Pathol* 2003; 24: 313 – 9.

(14.) Hoff CJB, Ratard R. Louisiana death certificate accuracy: a concern for the public's health. *J La State Med Soc* 2010; 162: 350 – 3.

(15.) Maudsley G, Williams EMI. 'Inaccuracy' in death certification - where are we now ? *J Public Heal Med* 1996; 18: 59 – 66.

(16.) Madea B, Argo A. Certification of Death: External Postmortem Examination. In: *Handbook of Forensic Medicine*. 2014, pp. 57 – 74.

(17.) Carpenter B, Tait G. The Autopsy Imperative: Medicine, law, and the coronial investigation. *J Med Humanit* 2010; 31: 205 – 21.

(18.) Hanzlick R. *Cause of death and death certificate. Important information for physicians, coroners, medical examiners and the public.* 2006.

(19.) Komolafe AO, Komolafe AO. Examining the crucial components of quality in clinical autopsies : reflections as correlates of quality health care and implications for health professionals. *Asian Arch Pathol* 2022; 4: 5 – 19.

(20.) Komolafe AO. Guiding principles and laws in the interpretation of postmortem findings. *Int Clin Pathol J* 2018; 6: 186 – 90.

(21.) Komolafe Akinwumi Oluwole, Adefidipe Adeyemi Abiola, Akinyemi Hezekiah AM, et al. Emphasising the Importance and Evaluation of Contributions of Pre-Morbid Disorders to Death in Medicolegal Autopsies. *Niger J Heal Sci* 2019; 19: 9 – 13.

(22.) Banwari M. An erroneous opinion on a cause of death in a forensic autopsy : a case report . *Afr Health Sci* 2017; 17: 1246 – 9.

(23.) Meyers S. Educational Case: Death Certification and the Role of the Medical Examiner/Coroner. *Acad Pathol* 2018; 5: 2374289517724724. doi: 10.1177/2374289517724724.

(24.) Kanchan T, Krishan K. *Forensic Pathology - Principles and Overview*. 2nd ed. Elsevier Ltd. Epub ahead of print 2012. DOI: 10.1016/B978-0-12-382165-2.00183-5.

(25.) Hanzlick R. Quality assurance review of death certificates: A pilot study. *Am J Forensic Med Pathol* 2005; 26: 63 – 5.

(26.) Morgan A, Andrew T, Guerra SMA, et al. Provider reported challenges with completing death certificates: A focus group study demonstrating potential sources of error. *PLoS One* 2022; 17: 1 – 12.

(27.) Nadesan K. The importance of the medico-legal autopsy. *The Malays J Pathol* 1997; 19: 105 – 9.

(28.) Ravakhah K. Death certificates are not reliable: Revivification of the autopsy. *South Med J* 2006; 99: 728 – 33.

(29.) Thorning D. The role of autopsy in the prevention of medical errors. *Lab Med* 2001; 32: 248 – 9.

(30.) Komolafe A.O.; Titiloye N.A. Essentials of Autopsy Pathology. *Niger J Fam Pract* 2016; 7: 7 – 14.

(31.) Komolafe AO. The Morphological Basis and Laws of Autopsy Interpretation: Exploring the Relationship between the Basic Medical Sciences, Anatomical Pathology and Clinical Practice. In: Sheriff D.S. (ed) *Current Trends in Medicine and Medical Research Vol. 4*. West Bengal: Book Publisher International, 2019, pp. 74 – 9.

(32.) Medical certification of cause of death. Instructions for physicians on use of international form of medical certificate of cause of death. Geneva. World Health Organization. 1979. Available from: https://www.google.com/search?client=firefox-b-d&q=medical+certification+of+cause+of+death. Accessed on 25th March 2023

(33.) Kotabagi RB, Chaturvedi RK, Banerjee A. Medical certification of cause of death. *Med J Armed Forces India* 2004; 60: 261 – 72.

(34.) Alsop K, Thorne H, Sandhu S, et al. A community-based model of rapid autopsy in end-stage cancer patients. *Nat Biotechnol* 2016; 34: 1010 – 4.

(35.) Engelmann C, Clària J, Szabo G, et al. Pathophysiology of decompensated cirrhosis: Portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction. *J Hepatol* 2021; 75: S49 – 66.

(36.) Panella MJ. Death investigation liability of medical examiners and coroners. *J Leg Med* 2011; 32: 449 – 81.

(37.) Kemp WL, Barnard JJ. Forensic Pathology. In: *Cheng L., Bostwick DG, Essentials of Anatomic Pathology 4th Ed. Springer, New York.* 2016, pp. 448 – 9.

(38.) Makary MA, Daniel M. Medical error-the third leading cause of death in the US. *BMJ* 2016; 353: 1 – 5.

(39.) LawTeacher. R v Adomako - 1995 [Internet]. November 2013. [Accessed 2 November 2024]; Available from: https://www.lawteacher.net/cases/r-v-adomako.php?vref=1.

(40.) Robson M, Maskill J, Brookbanks W. Doctors Are Aggrieved—Should They Be? Gross Negligence Manslaughter and the Culpable Doctor. *J Crim Law* 2020; 84: 312 – 40.

(41.) Below E, Lignitz E. Cases of fatal poisoning in post-mortem examinations at the Institute of Forensic Medicine in Greifswald - Analysis of five decades of post-mortems. In: *Forensic Science International*. 2003, pp. 125 – 131.

(42.) Davis GG. *Pathology and Law*. 2004. Epub ahead of print 2004. DOI: 10.1007/978-0-387-21818-2.

APPENDIX 1
INFORMATION FOR AUTHORS

All authors listed in a paper submitted to Asian Archives of Pathology (AAP) must have contributed substantially to the work. It is the corresponding author who takes responsibility for obtaining permission from all co-authors for the submission. When submitting the paper, the corresponding author is encouraged to indicate the specific contributions of all authors (the author statement, with signatures from all authors and percentage of each contribution can be accepted). Examples of contributions include: designed research, performed research, contributed vital new reagents or analytical tools, analysed data, and wrote the paper. An author may list more than one type of contribution, and more than one author may have contributed to the same aspect of the work.

Authors should take care to exclude overlap and duplication in papers dealing with related materials. See also paragraph on Redundant or Duplicate Publication in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" at http://www.icmje.org/index.html.

The submitted manuscripts will be reviewed by the members of the Editorial Board or the expert reviewers. At the discretion of the Editorial Board, the manuscripts may be returned immediately without full review, if deemed not competitive or outside the realm of interests of the majority of the readership of the Journal. The decision (reject, invite revision, and accept) letter will be coming from the Editorial Board who has assumed responsibility for the manuscript's review. The editor's decision is based not just on technical merit of the work, but also on other factors such as the priority for publication and the relevance to the Journal's general readership. All papers are judged in relation to other submissions currently under consideration.

Categories of Manuscripts

1. Letters to the Editor

The letters to the editor are the reactions to any papers published in AAP. These letters will be reviewed by the Editorial Board and sent to the authors of the original paper with an invitation to respond. Letters and eventual responses will be published together, when appropriate.

- *Word Count: 300 – 500 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figure or Table: Maximum of 1 (if needed)*

2. Original Articles

The original articles are the researches describing the novel understanding of anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal medicine or medical jurisprudence), molecular medicine or pathobiology. Systematic reviews, meta-analyses and clinical trials are classified as articles. The articles should be clearly and concisely written in the well-organised form (see ***Organisation of Manuscripts***): abstract; introduction; materials and methods; results; discussion; and conclusions. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two or more experts in the field.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Structured Abstract (see* ***Organisation of Manuscripts****): 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 6*

3. Review Articles

The review articles are generally invited by the Editor-in-Chief. They should focus on a topic of broad scientific interest and on recent advances. These articles are peer-reviewed before the final decision to accept or reject the manuscript for publication. Therefore, revisions may be required.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 4*

4. Case Reports

AAP limits publication of case reports to those that are truly novel, unexpected or unusual, provide new information about anatomical pathology, clinical pathology (laboratory medicine) or forensic medicine (legal medicine or medical jurisprudence). In addition, they must have educational value for the aforementioned fields. The journal will not consider case reports describing preventive or therapeutic interventions, as these generally require stronger evidence. Case reports that involve a substantial literature review should be submitted as a review article. The submitted case reports will undergo the usual peer-reviewed process.

- *Word Count: 1,200 – 2,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 20*
- *Figures or Tables: Maximum of 4*

5. Case Illustrations

Case illustrations are aimed to provide education to readers through multidisciplinary clinicopathological discussions of interesting cases. The manuscript consists of a clinical presentation or description, laboratory investigations, discussion, final diagnosis, and up to 5 take-home messages (learning points). Regarding continuous learning through self-assessment, each of the case illustrations will contain 3 – 5 multiple choice questions (MCQs) with 4 – 5 suggested answers for each question. These MCQs are placed after the final diagnosis and the correct answers should be revealed after the references. The questions and take-home messages (learning points) are included in the total word count. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two experts in the field.

- *Word Count: 1,000 – 2,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figures: Maximum of 2*

- *Tables: Maximum of 5*

6. Technical Notes

The technical notes are brief descriptions of scientific techniques used in the anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal medicine or medical jurisprudence), molecular medicine or pathobiology. The submitted manuscripts are usually peer-reviewed.

- *Word Count: Maximum of 1,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 5*
- *Figures or Tables: Maximum of 2*

Organisation of Manuscripts

1. General Format

The manuscripts written in English language are preferable. However, Thai papers are also acceptable, but their title pages, abstracts, and keywords must contain both Thai and English. These English and Thai manuscripts are prepared in A4-sized Microsoft Word documents with leaving 2.54-cm (1-inch) margins on all sides. All documents are required to be aligned left and double-spaced throughout the entire manuscript. The text should be typed in 12-point regular Times New Roman font for English manuscript and 16-point regular TH SarabunPSK font for Thai manuscript.

The running titles of English and Thai manuscripts are placed in the top left-hand corner of each page. They cannot exceed 50 characters, including spaces between words and punctuation. For the header of English paper, the running title will be typed in all capital letters. The page number goes on the top right-hand corner.

Footnotes are not used in the manuscripts, but parenthetical statements within text are applied instead and sparingly. Abbreviations should be defined at first mention and thereafter used consistently throughout the article. The standard abbreviations for units of measure must be used in conjunction with numbers.

All studies that involve human subjects should not mention subjects' identifying information (e.g. initials) unless the information is essential for scientific purposes and the patients (or parents or guardians) give written informed consent for publication.

2. Title Page

The title page is the first page of the manuscripts and must contain the following:

- The title of the paper (not more than 150 characters, including spaces between words)
- The full names, institutional addresses, and email addresses for all authors (If authors regard it as essential to indicate that two or more co-authors are equal in status, they may be identified by an asterisk symbol with the caption “These authors contributed equally to this work” immediately under the address list.)
- The name, surname, full postal address, telephone number, facsimile number, and email address of the corresponding author who will take primary responsibility for communication with AAP.
- Conflict of interest statement (If there are no conflicts of interest for any author, the following statement should be inserted: “The authors declare that they have no conflicts of interest with the contents of this article.”)

3. Abstract

A structured form of abstract is used in all Original Article manuscripts and must include the following separate sections:

- *Background: The main context of the study*
- *Objective: The main purpose of the study*
- *Materials and Methods: How the study was performed*
- *Results: The main findings*
- *Conclusions: Brief summary and potential implications*
- *Keywords: 3 – 5 words or phrases (listed in alphabetical order) representing the main content of the article*

4. Introduction

The Introduction section should clearly explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

5. Materials and Methods

The Materials and Methods section must be described in sufficient detail to allow the experiments or data collection to be reproduced by others. Common routine methods that have been published in detail elsewhere should not be described in detail. They need only be described in outline with an appropriate reference to a full description. Authors should provide the names of the manufacturers and their locations for any specifically named medical equipment and instruments, and all chemicals and drugs should be identified by their systematic and pharmaceutical names, and by their trivial and trade names if relevant, respectively. Calculations and the statistical methods employed must be described in this section.

All studies involving animal or human subjects must abide by the rules of the appropriate Internal Review Board and the tenets of the recently revised Helsinki protocol. Hence, the manuscripts must include the name of the ethics committee that approved the study and the committee's reference number if appropriate.

6. Results

The Results section should concisely describe the findings of the study including, if appropriate, results of statistical analysis which must be presented either in the text or as tables and figures. It should follow a logical sequence. However, the description of results should not simply repeat the data that appear in tables and figures and, likewise, the same

data should not be displayed in both tables and figures. Any chemical equations, structural formulas or mathematical equations should be placed between successive lines of text. The authors do not discuss the results or draw any conclusions in this section.

7. Discussion

The Discussion section should focus on the interpretation and the significance of the findings against the background of existing knowledge. The discussion should not repeat information in the results. The authors will clearly identify any aspects that are novel. In addition, there is the relation between the results and other work in the area.

8. Conclusions

The Conclusions section should state clearly the main summaries and provide an explanation of the importance and relevance of the study reported. The author will also describe some indication of the direction future research should take.

9. Acknowledgements

The Acknowledgements section should be any brief notes of thanks to the following:

- *Funding sources*
- *A person who provided purely technical help or writing assistance*
- *A department chair who provided only general support*
- *Sources of material (e.g. novel drugs) not available commercially*

Thanks to anonymous reviewers are not allowed. If you do not have anyone to acknowledge, please write “Not applicable” in this section.

10. References

The Vancouver system of referencing should be used in the manuscripts. References should be cited numerically in the order they appear in the text. The authors should identify references in text, tables, and legends by Arabic numerals in parentheses or as superscripts. Please give names of all authors and editors. The references should be numbered and listed in order of appearance in the text. The names of all authors are cited when there are six or fewer. When there are seven or more, only the first three followed by “et al.” should be given. The names of journals should be abbreviated in the style used in Index Medicus (see examples below). Reference to unpublished data and personal

communications should not appear in the list but should be cited in the text only (e.g. A Smith, unpubl. Data, 2000).

- *Journal article*
  1. Sibai BM. Magnesium sulfate is the ideal anticonvulsant in preeclampsia – eclampsia. Am J Obstet Gynecol 1990; 162: 1141 – 5.
- *Books*
  2. Remington JS, Swartz MN. Current Topics in Infectious Diseases, Vol 21. Boston: Blackwell Science Publication, 2001.
- *Chapter in a book*
  3. Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Bloom SL, Wenstrom KD. Hypertensive disorders in pregnancy. In: Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Brom SL, Wenstrom KD, eds. Williams Obstetrics, 22nd ed. New York: McGraw-Hill, 2005: 761 – 808.

11. Tables

The tables should be self-contained and complement, but without duplication, information contained in the text. They should be numbered consecutively in Arabic numerals (Table 1, Table 2, etc.). Each table should be presented on a separate page with a comprehensive but concise legend above the table. The tables should be double-spaced and vertical lines should not be used to separate the columns. The column headings should be brief, with units of measurement in parentheses. All abbreviations should be defined in footnotes. The tables and their legends and footnotes should be understandable without reference to the text. The authors should ensure that the data in the tables are consistent with those cited in the relevant places in the text, totals add up correctly, and percentages have been calculated correctly.

12. Figure Legends

The legends should be self-explanatory and typed on a separate page titled “Figure Legends”. They should incorporate definitions of any symbols used and all abbreviations and units of measurement should be explained so that the figures and their legends are understandable without reference to the text.

If the tables or figures have been published before, the authors must obtain written permission to reproduce the materials in both print and electronic formats from the copyright owner and submit them with the manuscripts. These also follow for quotes, illustrations, and other materials taken from previously published works not in the public domain. The original resources should be cited in the figure captions or table footnotes.

13. Figures

All illustrations (line drawings and photographs) are classified as figures. The figures should be numbered consecutively in Arabic numerals (Figure 1, Figure 2, etc.). They are submitted electronically along with the manuscripts. These figures should be referred to specifically in the text of the papers but should not be embedded within the text. The following information must be stated to each microscopic image: staining method, magnification (especially for electron micrograph), and numerical aperture of the objective lens. The authors are encouraged to use digital images (at least 300 d.p.i.) in .jpg or .tif formats. The use of three-dimensional histograms is strongly discouraged when the addition of these histograms gives no extra information.

14. Components

14.1. Letters to the Editor

The Letter to the Editor manuscripts consist of the following order:

- *Title Page*
- *Main Text*
- *References*
- *Table (if needed)*
- *Figure Legend (if needed)*
- *Figure (if needed)*

14.2. Original Articles

The Original Article manuscripts consist of the following order:

- *Title Page*
- *Structured Abstract*
- *Introduction*
- *Materials and Methods*
- *Results*
- *Discussion*
- *Conclusions*
- *Acknowledgements*

- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.3. Review Articles

The Review Article manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Main Text*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.4. Case Reports

The Case Report manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Case Description*
- *Discussion*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.5. Case Illustrations

The Case Illustration manuscripts consist of the following order:

- *Title Page*
- *Clinical Presentation or Description*
- *Laboratory Investigations*
- *Discussion*
- *Final Diagnosis*
- *Multiple Choice Questions (MCQs)*
- *Take-Home Messages (Learning Points)*
- *Acknowledgements*
- *References*
- *Correct Answers to MCQs*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.6. Technical Notes

The Technical Note manuscripts consist of the following order:

- *Title Page*
- *Introduction*
- *Main text*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

Proofreading

The authors of the accepted manuscripts will receive proofs and are responsible for proofreading and checking the entire article, including tables, figures, and references. These authors should correct only typesetting errors at this stage and may be charged for extensive alterations. Page proofs must be returned within 48 hours to avoid delays in publication.

Revised Manuscripts

In many cases, the authors will be invited to make revisions to their manuscripts. The revised manuscripts must generally be received by the Editorial Board within 3 months of the date on the decision letter or they will be considered a new submission. An extension can sometimes be negotiated with the Editorial Board.

APPENDIX 2
BENEFITS OF PUBLISHING WITH ASIAN ARCHIVES OF PATHOLOGY

Asian Archives of Pathology (AAP) is an open access journal. Open Access makes your works freely available to everyone in the world. It provides a significant boost to the readership of your articles, and has been shown to have an increase in positive influence on citations and reuse. Hence, open-access leads to more recognition for our esteemed authors.

The journal has been sponsored by the Royal College of Pathologists of Thailand. We have the policy to disseminate the verified scientific knowledge to the public on a non-profit basis. Hence, we have not charged the authors whose manuscripts have been submitted or accepted for publication in our journal.

Since AAP is also a peer-reviewed journal, the submitted manuscripts will be reviewed by the members of the Editorial Board or the expert reviewers. The decision on these manuscripts is processed very fast without any delay and in shortest possible time. The processing period is 1–2 weeks. These decisions of the reviewers are unbiased and the decision (reject, invite revision, and accept) letter coming from the Editorial Board is always conveyed to the authors.

APPENDIX 3
SUBMISSION OF THE MANUSCRIPTS

Step 1: Access www.asianarchpath.com

Step 2: If you did not register before, please create an account first.

Step 3: Login with your username and password.

Step 4: Click the "+ New Submission" button on the upper right-hand side of the page.

Step 5: Proceed to fill up the Submission Form online and follow the directions given therein.

Step 6: Upload your manuscript file (s).

Step 7: Re-check the content of your manuscript (s) and the uploaded file (s) more carefully prior to the submission. If you have submitted your manuscript file (s) incorrectly, you must contact Editor-in-Chief of Asian Archives of Pathology immediately. The Editor-in-Chief can clear the incorrect attempt and allow you another submission.

Step 8: Click the "Submit Manuscript" button under Important Notice.

If you have any further enquiries, please do not hesitate to contact the Journal.

APPENDIX 4
CONTACT THE JOURNAL

The Editorial Office of Asian Archives of Pathology

Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
317 Rajavithi Road, Rajadevi, Bangkok 10400 Thailand

Telephone: +66 (0) 90 132 2047

Fax: +66 (0) 2 354 7791

Email: editor@asianarchpath.com

APPENDIX 5
SUPPORT THE JOURNAL

Asian Archives of Pathology (AAP) has a mission of disseminating the unbiased and reliable medical knowledge on a non-profit basis. If you consider that this journal is useful for the public, you can support us by submitting your advertisements via the contact information below.

Assistant Professor Dr Chetana Ruangpratheep
The Editorial Office of Asian Archives of Pathology
Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
317 Rajavithi Road, Rajadevi, Bangkok 10400 Thailand
Telephone: +66 (0) 90 132 2047
Fax: +66 (0) 2 354 7791

Email: editor@asianarchpath.com

Every support, small or big, can make a difference.

Thank you

Assistant Professor Dr Chetana Ruangpratheep

MD, FRCPath (Thailand), MSc, PhD

Editor-in-Chief of Asian Archives of Pathology

ACADEMIC MEETINGS AND CONFERENCES

Announcements of academic meetings and conferences that are of interest to the readers of Asian Archives of Pathology (AAP) should be sent to the Editor-in-Chief at least 3 months before the first day of the month of issue. The contact information is shown below.

Assistant Professor Dr Chetana Ruangpratheep
The Editorial Office of Asian Archives of Pathology
Department of Pathology, Floor 6, Her Royal Highness Princess Bejaratana Building
Phramongkutklao College of Medicine
317 Rajavithi Road, Rajadevi, Bangkok 10400 Thailand

Telephone: +66 (0) 90 132 2047

Fax: +66 (0) 2 354 7791

Email: editor@asianarchpath.com

WHAT IS INSIDE THIS ISSUE?

Original Article:

Review Article: