

## BRIEF REPORTS

## Causes of Sudden Unexpected Death of Adult Hospital Patients

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The sudden unexpected death of a hospitalized patient is distressing to the family and the healthcare team. It is also common. Assessment of the causes without autopsy is frequently incorrect. To elucidate the causes of death, 175 cases of adult hospital patients in the University of Pittsburgh Medical Center Health System, who died suddenly and unexpectedly, were investigated with autopsies. The most common cause was judged to be a cardiac arrhythmia, in 58 (33%) of cases, presumptive in 46 cases, because only 12 of these patients were on cardiac monitoring. Of the arrhythmia patients, 36 (62%) had  $\geq 75\%$  coronary artery stenosis and 31

(53%) had histological evidence of myocardial infarction, with 15 (26%) of those with subacute or old myocardial infarction lacking a history of myocardial infarction. Hemorrhage was judged the cause of death in 38 (22%) of cases, including 31 (82%) with endogenous coagulopathy, anticoagulation, or antiplatelet therapy. Pulmonary thromboembolism was judged the cause of death in 27 (15%) of cases. Overall, hemorrhage deserves better appreciation as a cause of sudden unexpected death of hospitalized adults. *Journal of Hospital Medicine* 2012;7:706–708. © 2012 Society of Hospital Medicine

The sudden unexpected death of a hospitalized patient is extremely distressing to the family and the healthcare team. It is also distressingly common. Over 200,000 treated cardiac arrests are estimated to occur each year in US hospital patients.<sup>1</sup> Most of these patients die, and studies have shown that physicians often incorrectly diagnose the causes of death when autopsies are performed to determine the causes of death.<sup>2,3</sup> This study was undertaken to elucidate the causes of sudden unexpected death of adult hospital patients as determined by autopsy.

## METHODS

One hundred seventy-five consecutive cases with autopsies by the senior author (L.N.) of adult hospital patients in the University of Pittsburgh Medical Center (UPMC) Health System, who died within 1 hour after onset of symptoms and in which death was unexpected, were retrospectively analyzed. Patients under 18, or dead on arrival, or on comfort measures only, were excluded. The unexpectedness of the deaths in this series was determined by review of the medical record, usually confirmed by a pre-autopsy discussion with a clinician (following UPMC policy), and by the fact that attempted resuscitation was carried out in all but a few cases. Patient age, sex, race, and causes of death were obtained from the autopsy report. The medical record was reviewed to determine if the patient was on cardiac mon-

itoring at the time of death. The study was approved by the University of Pittsburgh Medical Center Committee for Oversight of Research Involving the Dead.

## RESULTS

The 175 autopsies in this study included 98 male patients and 77 female patients. Their ages ranged from 19 to 95 years, with an average age of 63.8 years. Categorized by race, 139 were white, 34 black, 1 Hispanic, and 1 Filipino. The autopsies were done over a 14-year period from 1992 to 2006, during which the autopsy rate gradually decreased from 19% to 8%. Seeking authorization for autopsy from family was the responsibility of clinicians.

The most common immediate cause of death was judged to be a cardiac arrhythmia, usually presumptive; this was the immediate cause of death in 58 (33.1%) cases, as shown in Table 1. Second most common was hemorrhage, which was the immediate cause of death in 38 (21.7%) cases, and third was pulmonary thromboembolism in 27 (15.4%) cases, as shown in Table 1. Other conditions judged to be the immediate cause of death were cardiogenic pulmonary edema/congestive heart failure in 13 cases (7.4%), sepsis in 11 cases (6.3%), pulmonary edema due to acute lung injury in 4 cases (3 with associated pneumonia), and acute respiratory failure due to pneumonia (in 3 cases), usual interstitial pneumonia (2), emphysema (1), chronic obstructive pulmonary disease (1), herpes simplex virus bronchitis (1), carbon dioxide narcosis (1), and undiagnosed massive metastatic pancreatic carcinoma infiltrating and pushing up the diaphragm (1). Miscellaneous other conditions judged to be the immediate cause of death were brain stem compression in 2 cases, aspiration in 2 cases, and—in 1 case each—subarachnoid hemorrhage, hemorrhagic cerebral infarction, fat embolism, amniotic fluid

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embolism, bilateral pneumothoraces, massive hemolysis, sickle cell vaso-occlusive crisis, cardiopulmonary decompensation, cardiac tamponade (due to pericardial metastases), and shock and systemic inflammatory response syndrome (due to volvulus).

The majority, 36 of the 58 patients (62%), with sudden death judged due to arrhythmias, had 75% or greater stenosis of 1 or more coronary arteries (average 2); 11 of these patients were on cardiac monitoring with their fatal arrhythmia displayed on the monitor, and 1 patient was wearing a Holter monitor at the time of her sudden death. The frequency of cardiac arrhythmia as a cause of sudden death did not change over the course of the 14 years of this study. Among the 31 of the 58 patients (53.4%) with histologically confirmed myocardial infarctions, 15 (25.9%) had a remote or subacute myocardial infarction without a history of myocardial infarction.

The most common underlying cause of death was severe coronary atherosclerosis, as shown in Table 2, but there were 14 patients whose underlying cause of death was a diverse group of other heart diseases. Five patients died postoperatively following heart surgery. One patient had a mitral valve papillary

fibroelastoma, and another patient's arrhythmia was preceded by a right bundle branch block and a new first-degree atrioventricular block attributable to mitral annular calcification. One patient with sickle cell disease had a myocardial bridge over a coronary artery. Three patients had heart transplants, 2 alcoholic cardiomyopathy, and 1 idiopathic dilated cardiomyopathy.

The initial cardiac rhythm during attempted cardiopulmonary resuscitation was obtainable for 120 cases. As shown in Table 3, a higher proportion of patients judged to have died of arrhythmias had an initial rhythm of ventricular tachycardia or fibrillation than the proportion of those judged to have died of hemorrhage, pulmonary embolism, or other immediate causes of death.

## DISCUSSION

The patients who had an initial cardiac rhythm of asystole during attempted resuscitation, and were judged to have died of an arrhythmia, most likely had ventricular tachycardia or some other arrhythmia before asystole. The majority of them were found in cardiac arrest at night, not on cardiac monitoring. In other studies, there has been an unexplained continuing decline in the prevalence of sudden cardiac arrest cases presenting with ventricular fibrillation and corresponding rise in the prevalence of pulseless electrical activity (PEA) arrests.<sup>4</sup> The 7 patients who had an initial cardiac rhythm of PEA and were judged to have died of an arrhythmia were all, except 1, off cardiac monitoring. Four had myocardial infarctions, 3 heart block pre-arrest, 1 postoperative intramyocardial

**TABLE 1. Most Common Immediate Causes of Sudden Death in Adult Hospital Patients**

Immediate Cause of Death	No. (n = 175)
Cardiac arrhythmia	58 (33.1%)
With $\geq 75\%$ coronary stenosis	36
With myocardial infarction	31
Remote	23
Acute or subacute	13
Hemorrhage	38 (21.7%)
With endogenous coagulopathy	13
With oral or injected anticoagulation	12
With antiplatelet therapy	6
Site: Pericardial (tamponade)	15
Retroperitoneal	6
Airway	4
Gastrointestinal	4
Pleural space	2
Thoracoabdominal	2
Intra-abdominal	1
Mediastinal	1
Nasopharyngeal	1
Retroperitoneal and pleural	1
Multi-organ	1
Pulmonary thromboembolism	27 (15.4%)

**TABLE 2. Underlying Causes of Sudden Expected Death**

Underlying Cause of Death	No. (%) n = 175
Severe coronary atherosclerosis	43 (24.6)
Neoplastic disease	30 (17.1)
Various heart diseases (see text)	14 (8.0)
Digestive system disorders	14 (8.0)
Aortic aneurysm or dissection	12 (6.9)
Chronic lung disease	8 (4.6)
Infectious diseases	7 (4.0)
Autoimmune diseases	5 (2.9)
Diabetes mellitus	4 (2.3)
Deep vein thrombosis	3 (1.7)
Morbid obesity	3 (1.7)
Other	32 (18.3)

**TABLE 3. Initial Cardiac Rhythms With Attempted Cardiopulmonary Resuscitation**

Immediate Cause of Death	Initial Cardiac Rhythm, No. (%)				
	Ventricular Tachycardia/Fibrillation n = 28	Bradycardia n = 33	Pulseless Electrical Activity n = 21	Asystole n = 31	Total
Arrhythmia	14 (50)	6 (18)	7 (33)	16 (52)	43
Hemorrhage	6 (21)	10 (30)	10 (48)	6 (19)	32
Thromboembolism	2 (7)	8 (24)	2 (10)	2 (6)	15*
Other	6 (21)	9 (27)	2 (10)	7 (23)	30†

\* Includes 1 patient with sinus tachycardia.

† Includes 1 patient with paced rhythm and 1 with multifocal atrial tachycardia.

hematoma, 1 myocardial metastatic melanoma, 1 acute heart transplant rejection, and 3 ventricular tachycardia or fibrillation following PEA, suggesting that PEA was a phase in the evolution of an arrhythmogenic death. The patients who had an initial cardiac rhythm of ventricular tachycardia or fibrillation, and were judged to have died of hemorrhage or pulmonary thromboembolism, generally had coronary artery disease. The hemorrhage or embolism presumably caused terminal myocardial ischemia, but the cardiac disease was judged to be a contributing cause of death, less important than the immediate cause.

The conclusion that a cardiac arrhythmia was the most common mechanism of death in this series fits with the conclusion that cardiac arrhythmias were the most common immediate cause of cardiac arrest, specifically of 49% of them, in a study of 14,720 cardiac arrests of adult inpatients.<sup>5</sup> It is accepted by convention that the presence of 75% or greater cross-sectional luminal narrowing of a coronary artery, even without thrombosis, can be a cause of sudden cardiac death.<sup>6</sup> Cardiac arrhythmias commonly occur during myocardial ischemia prior to the irreversible necrosis of myocardial infarction.<sup>7</sup> Fatal cardiac arrhythmias can also be caused by old myocardial infarctions.<sup>8</sup> The finding that 15 of the patients in this study, 25.9% of the 58 whose sudden death was attributable to a cardiac arrhythmia, had a remote or subacute myocardial infarction without a history of myocardial infarction fits with evidence that 25%–30% of myocardial infarctions are unrecognized.

Hemorrhage has been an underpublicized cause of unexpected sudden death in hospital patients. Intracranial hemorrhages, due to ruptured berry aneurysms, hypertension, tumors, or arteriovenous malformations, are well-recognized causes of sudden death, but not specifically in hospital patients.<sup>9</sup> In a Scottish series of 111 unexpected sudden deaths due to an “acute abdomen” in patients aged 70 or older, 24 died of acute gastrointestinal hemorrhage, but cases of ruptured abdominal aortic aneurysm were excluded from the study because they would have dominated the analysis.<sup>10</sup> Retroperitoneal hemorrhage is a particularly insidious cause of sudden death. It commonly causes little or no pain, and proceeds asymptotically until the patient reaches the limits of cardiopulmonary compensation, which can mask the hemodynamic effect of the bleeding until sudden death.

The limitations of this study include the presumptive nature of the arrhythmias in the majority of patients judged most likely to have died of arrhythmias, and a potential selection bias in the cases coming to autopsy. No data on the 81% to 92% of deaths not investigated by autopsy is available, so the possibility of some sort of selection bias in this case series cannot be excluded. The causes of death determined by autopsy also inevitably represent a judgment or opinion about causation (as opposed to mere correlation), just as the assessment of the causes of death without

autopsy does, but autopsy adds the knowledge of conditions undiagnosed prior to death and the exclusion of some suspected diagnoses, substantially improving the unavoidably judgmental conclusion.

There are implications for preventing the sudden unexpected death of hospital patients from the results of this study. They suggest that more cardiac rhythm monitoring might be helpful.<sup>11</sup> More prophylactic antiarrhythmic medication and automatic implanted cardiac defibrillators might also be helpful.<sup>12</sup> Some UPMC intensivists believe that the sort of fatal arrhythmias seen in this study are caused by hypoxemia, which suggests that more pulse oximetry oxygen saturation monitoring might allow preventative intervention.<sup>13</sup> More frequent and possibly automated monitoring of vital signs might provide early warning of hemorrhage or pulmonary embolization.<sup>14</sup> Keeping a wide differential diagnosis is taught for resuscitation with an initial rhythm of PEA, but keeping a wide differential including hemorrhage in cases with other initial rhythms, especially bradycardia, for example, may be important. This study suggests the importance of keeping hemorrhage in the differential diagnosis of sudden unexpected cardiac arrest of hospital patients.

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## References

1. Merchant RM, Yang L, Becker LB, et al. Incidence of treated cardiac arrest in hospitalized patients in the United States. *Crit Care Med*. 2011;39:2401–2406.
2. Tavora F, Crowder CD, Chen-Chi S, Burke AP. Discrepancies between clinical and autopsy diagnoses. A comparison of university, community and private autopsy practices. *Am J Clin Pathol*. 2008; 129:102–109.
3. Heriot GS, Pitman AG, Gonzales M, McKelvie P. The four horsemen: clinicopathological correlation in 407 hospital autopsies. *Intern Med J*. 2010;40:626–632.
4. Teodorescu C, Reinier K, Dervan C, et al. Factors associated with pulseless electric activity versus ventricular fibrillation: the Oregon sudden unexpected death study. *Circulation*. 2010;122(21): 2116–2122.
5. Peberdy MA, Kaye W, Ornato JP, et al. Cardiopulmonary resuscitation of adults in the hospital: a report of 14,720 cardiac arrests from the national registry of cardiopulmonary resuscitation. *Resuscitation*. 2003;58:297–308.
6. Burke AP, Farb A, Virmani R. Coronary thrombosis: what's new? *Pathol Case Rev*. 2001;6:244–252.
7. Luqman N, Sung RJ, Wang CL, Kuo CT. Myocardial ischemia and ventricular fibrillation: pathophysiology and clinical implications. *Int J Cardiol*. 2007;119:283–290.
8. Mehta D, Curwin J, Gomes JA, Fuster V. Sudden death in coronary artery disease: acute ischemia versus myocardial substrate. *Circulation*. 1997;96:3215–3223.
9. Black M, Graham DI. Sudden unexplained death in adults. *Curr Top Pathol*. 2001;95:125–148.
10. Ng CY, Squires TJ, Busuttill A. Acute abdomen as a cause of death in sudden, unexpected deaths in the elderly. *Scott Med J*. 2006;52: 20–23.
11. Saxon LA. Survival after tachyarrhythmic arrest—what are we waiting for? *N Engl J Med*. 2008;358:77–79.
12. Ye S, Grunnert M, Thune JJ, et al. Circumstances and outcomes of sudden unexpected death in patients with high-risk myocardial infarction: implications for prevention. *Circulation*. 2011;123: 2674–2680.
13. Kline JA, Hernandez-Nino J, Newgard CD, Cowles DN, Jackson RE, Courtney DM. Use of pulse oximetry to predict in-hospital complications in normotensive patients with pulmonary embolism. *Am J Med*. 2003;115(3):203–208.
14. Orphanidou C, Clifton D, Khan S, Smith M, Feldmar J, Tarassenko L. Telemetry-based vital sign monitoring for ambulatory hospital patients. *Conf Proc IEEE Eng Med Biol Soc*. 2009;2009:4650–4653.