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Commentary

The Value of Autopsy in Modern Oncology

C. SETH LANDEFELD* and LEE GOLDMAN†

**Division of General Internal Medicine and the Clinical Analysis Project, Department of Medicine, University Hospitals of Cleveland and Case Western Reserve University School of Medicine, U.S.A. and †Division of Clinical Epidemiology, Consolidated Department of Medicine, Brigham and Women's and Beth Israel Hospitals and Harvard Medical School, Boston, U.S.A.*

(A COMMENT ON: McKay MJ, Langlands AO. On the yield of new information from selective requesting of *post mortem* examinations in oncology patients. *Eur J Cancer Clin Oncol* 1988, **24**, 1707–1714.)

THE AUTOPSY has a long and important role in advancing medical science and practice [1]. The clinical value of autopsy was established in the eighteenth century by Morgagni, who contrasted the sobering reality of *post mortem* findings to the 'uncontrolled optimism' of clinicians [2]. In the nineteenth century, autopsies performed by Virchow, Osler and other physicians advanced knowledge of many diseases, including pulmonary embolism and endocarditis [1, 3].

The autopsy has also become an important tool in monitoring and improving the quality of medical care [4]. The systematic identification of discrepancies between clinical diagnoses and autopsy findings was initiated by Cabot in his 1912 study of 'diagnostic pitfalls' identified in 3000 autopsies [5]. Several recent studies have shown that the yield of autopsies remains high: treatable, major unexpected findings, which if known *ante mortem* would likely have improved survival, have been discovered in 5–10% of cases; other major unexpected findings were revealed in another 10% of cases [6–9].

The autopsy has a rich tradition in oncology as well [10]. In the early twentieth century, European and American pathologists reported that the diagnosis of cancer was missed *ante mortem* in 20–33% of autopsy cases with cancer; conversely, in 8–9% of cases with a clinical diagnosis of cancer, no cancer was found *post mortem* [11]. In the 1940s, Willis found that cancer was missed clinically in 13% of 943 autopsy cases of cancer in a Melbourne hospital; cancer was not found at autopsy in 6% of cases with that clinical diagnosis [12]. In the 1960s at Boston City Hospital, Bauer and Robbins found that fatal cancer was missed in 16% of 2091 such cases undergoing autopsy [13]. However, data from the 1970s and 1980s indicate that the proportion of fatal cancers that were missed clinically has fallen to about 4% [6–8].

Autopsies have also shed light on important non-malignant diseases in cancer patients. Bauer and Robbins found that 24% of deaths in cancer patients were caused by non-malignant diseases [13]. Recently, we observed that cancer patients were no less likely than other patients to die of a non-malignant disease that was missed clinically; in several cases, autopsies found treatable fatal infections in patients with cancer [6, 7].

Recently, autopsy rates have fallen from 50% in the 1940s to 14% in 1985 despite many studies demonstrating the diagnostic yield of the autopsy [1, 6–9]. Many physicians have claimed that modern diagnostic technology has reduced the need for *post mortem* examination [1] and it has been suggested that routine autopsies are 'folly', especially in cancer patients [14].

In a previous issue of this Journal, McKay and Langlands have presented data relevant to the ongoing debate about the value of autopsies in cancer patients [15]. The authors reviewed 100 consecutive autopsies performed on cancer patients registered in their department of radiation oncology during a period when autopsies were requested only if a high yield of new information was expected. This represented an autopsy rate of 6.7% for eligible cases, although the autopsy rate for the patients remaining under the authors' care was much higher

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Reprint requests should be addressed to: C. Seth Landefeld, M.D., Division of General Internal Medicine, Department of Medicine, University Hospitals of Cleveland, 2074 Abington Road, Cleveland, OH 44106, U.S.A.

(23%). Among 83 cases for which comparisons to the clinical diagnoses were made, the cause of death was missed clinically in eight cases (10%). In only one case was the missed diagnosis thought to be treatable, although the case of missed cerebral mycosis should also have been treatable. In three patients, the autopsy changed the histologic diagnosis of the type of cancer and in six cases established the histologic diagnosis when none had previously been available. In the assessment of the presence or absence of disease at sites treated with radical radiotherapy with curative intent, clinical diagnosis was inaccurate in five of 43 evaluated sites (12%). Thus, from the standpoint of the quality-control of diagnostic accuracy, these 83 autopsies apparently yielded significant new information in 22 instances. Nevertheless, McKay and Langlands thought their autopsies were 'low yield' and argued that (a) autopsy should be requested only in highly selected cases and (b) when autopsy is performed, a more directed, problem-oriented approach should be taken to improve the yield of new information.

We disagree with the conclusion that, in patients with a clinical diagnosis of cancer, autopsy should be requested only in *highly* selected cases. Such a policy may needlessly decrease the benefit of autopsies in these patients and cannot be based on the reported findings for the following reasons.

First, the external validity, or generalizability, of the study is limited by the fact that the eligible patients are representative not of all cancer patients but of a selected group of patients, namely those referred to a department of radiation oncology. It is possible, for example, that cancer patients referred for radiotherapy are more likely to have a well established diagnosis than are other patients with a clinical diagnosis of cancer. Thus, McKay and Langlands' finding that cancer was not found at autopsy in only 1% of their cases, as opposed to 6–9% in earlier series [11–13], may reflect the idiosyncracies of their referral population rather than more accurate diagnosis of cancer in all clinical practice.

Second, the method used for classifying diagnostic error may have systematically underestimated the clinical significance of autopsy findings. We have developed and applied a method for identifying and distinguishing between treatable major unexpected findings, which if known *ante mortem* would probably have improved survival, and untreatable major unexpected findings [6, 7, 9]. We recognize a subjective element in any judgment about the relevance of autopsy findings, especially in patients for which treatment is usually life-prolonging rather than life-saving, but our detailed method was designed to minimize this subjectivity. Applying our criteria, it is possible that the patients with cerebral mycosis, paracolic abscess, subdural hematoma, and renal infarct may have represented major unexpected findings, thus demonstrating a yield close to that expected on the basis of past reports [6–9]. The apparent difference in yield that could be related to the method of measurement underscores the need to adopt a reasonable but standard methodology based on detailed criteria.

Third, we disagree on what is likely to happen to the percentage yield of the autopsy when the autopsy rate rises. In a recent prospective study, we found that neither physicians nor clinical findings could reliably identify high-yield autopsy cases [7]. Furthermore, other investigators have observed that the yield of autopsy is fairly constant among studies in which autopsy rates have varied from 25% to 75% [9]. Thus, it is unclear whether the non-random selection of autopsy cases increased, decreased, or did not affect the apparent yield of autopsy in this study.

Finally, there is the issue of interpretation: what yield is high enough to warrant an autopsy? Clearly, there is no right answer to this question, but we believe a yield of major unexpected findings in even 10% of cases is important. The cost of autopsy is significant and adequate data should be obtained for the calculation of formal cost-effectiveness ratios. It would be tragic, however, if a measure of quality as valuable as the autopsy were to be abandoned because of cost. The cost of autopsy should be recognized as a necessary price for measuring and maintaining quality, not just an expense for research or education. Resources should be directed toward making autopsies as effective and efficient as possible in measuring and improving the quality of care; this will provide the basis for determining the cost-effectiveness of autopsies. Efforts in this area might include (1) evaluation of goal-oriented autopsies, (2) consideration of issues related to non-random case selection, (3) development and agreement on a standard method for classifying discrepancies between clinical diagnoses and autopsy findings, and (4) development of methods to use autopsy findings systematically to improve the quality of care.

Viewed in the context of past studies, the findings of McKay and Langlands in a selected sample of cancer patients referred for radiotherapy document both the continuing value of autopsy in cancer patients and the opportunity to improve the way in which autopsies are used in clinical medicine. Pending resolution of several specific issues that require further investigation, we believe that clinical oncologists, like other physicians, should obtain autopsies in all patients in whom there is reasonable clinical uncertainty and in a random sample of other cases, aiming for a rate of at least the 23% that

McKay and Langlands achieved. Goal-directed autopsies should be emphasized, and autopsy findings should be used systematically to improve the quality of care.

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