



Vera Peters and the conservative management of early-stage breast cancer

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ABSTRACT

During the first three quarters of the twentieth century, radical mastectomy was an accepted and common procedure in the management of patients with early-stage cancer of the breast. After a lifetime of thinking about and working with patients with early-stage breast cancer, Vera Peters presented and published, in the mid-1970s, a retrospective historical case-control study that demonstrated the lack of a survival benefit for radical or modified radical mastectomy as compared with more conservative surgery with lumpectomy. In the years that followed, prospective randomized studies confirmed her findings.

KEY WORDS

Vera Peters, cancer of the breast, early stage, radical mastectomy, lumpectomy, survival

1. INTRODUCTION

The early life and work of Vera Peters in the evaluation and treatment of patients with Hodgkin disease have been reviewed in this journal, and her contributions in that disease are widely recognized¹. However, Peters had another passion, and that was breast cancer—particularly, breast-conserving surgery in patients with early-stage cancer of the breast. This interest extended throughout her career, during which time, radical surgical treatment was the popular method of management.

2. BACKGROUND AND RADICAL MASTECTOMY

Extensive surgery for cancer of the breast was common in Europe as early as the mid-nineteenth century². However, particularly in North America, Dr. William S. Halsted has been given the credit for popularizing the radical mastectomy that became known as the “Halsted procedure”³. This physically deforming operation involved removal of the breast tissue, skin, nipple, axillary lymph nodes,

and sometimes the supraclavicular lymph nodes and the underlying chest wall muscles. It caused a great deal of psychological upset in many who underwent the procedure. The prevailing philosophy among surgeons of the time was that cancer spreads in a centrifugal manner from the primary lesion; thus, the more tissue surrounding the tumour that was removed, the higher the likelihood of cure.

The first exposure that Vera Peters had to breast cancer was when her mother developed the disease. It was progressive, and Mrs. Peters subsequently died in 1933 of metastatic disease when Vera was in her second-last year of medical school. The experience had a profound effect on Vera and influenced her career path and her interest in cancer of the breast⁴. The experience also introduced her to her future teacher and mentor: Dr. Gordon E. Richards, who treated Mrs. Peters with radiation.

After graduation and internship, Peters joined Richards in 1935 at the Ontario Radiotherapy Institute at the Toronto General Hospital, first as a trainee and later as member of his department. Aside from skin cancer, breast cancer was the most common malignancy referred to the Institute⁵, and 65% of breast cancer patients in Ontario underwent radical mastectomy⁶. Peters's chief, Dr. Richards, was committed to the procedure, and in a 1948 publication, he described the radical mastectomy as “one of the most perfect procedures in the whole field of surgery”⁷. Peters had adequate opportunity to witness the disfiguring results.

In later years, she wrote about the “resulting [physical] deformity” of mastectomy and also the “serious emotional impact” it had on patients⁸. She also spoke of the unpleasant experiences she had had relating to the “diverse devastations of breast cancer patients and how this inspired her to look to better methods [of treatment]”⁹.

3. THE MOVE TOWARD MORE CONSERVATIVE BREAST SURGERY

In a 1953 paper¹⁰, Peters reported that the largest group of patients referred to the Radiotherapy

Institute in Toronto fell into the radical mastectomy category. However, a gradually increasing number were coming with simple mastectomy, especially after McWhirter reported in 1948 “equally as good five and ten year survival irradiating carcinoma of the breast after simple mastectomy as following radical mastectomy”¹¹. Peters commented, “We are not entirely convinced that [simple mastectomy] is the method of choice for all breast cancers but we have fallen heir to a small series of cases ... and hope to report on it in the near future”¹⁰. The seed was sown for Peters to study less-aggressive therapy.

A number of events pushed the process on its way in Toronto. More patients were referred to the Institute who, for a variety of reasons—medical and otherwise—underwent excision of the tumour only (“lumpectomy”). Some patients received limited surgery because of advanced age and poor general health. A few patients refused radical surgery, and in addition, as evidence accumulated suggesting that conservative treatment might be as effective as radical surgery, several surgeons accepted that possibility. As recorded by Peters, “the impetus to change to the most conservative treatment (lumpectomy) was provided by a handful of patients and a few missionary surgeons. The patients were rebels against radical surgery ... insisting on removal of the lump, nearly always done against [their] surgeon’s wishes”¹². Peters became known as a radiation oncologist who cared for these patients in a sensitive manner. More and more patients with removal of the lump only were referred to her for radiation.

In the meantime, the literature (initially from Europe and Great Britain) began to throw some doubt on the dogma for radical surgery. In addition to McWhirter’s paper in 1948¹¹, other reports and opinions suggested that local treatment resulted in survival equivalent to that in patients who were treated by the more radical method. As early as 1937, Keynes was convinced that treatment of early breast cancer with a palisade of interstitial radium needles around the primary tumour site (surgically biopsied or locally removed) was as effective as radical surgery¹³. Mustakallio, a Finnish radiation oncologist, reported on 127 patients without significant axillary nodes who were treated by extirpation of the tumour only, followed by postoperative radiotherapy: the results were comparable to those obtained with more aggressive surgery¹⁴. Smithers, an international authority in oncology and radiation treatment, suggested in 1958 that “the settled days when the Halsted radical mastectomy was widely accepted as the only effective treatment for cancer of the breast are past”¹⁵.

In 1964, Porrit reported on a 1953 study by registrars at St. Bartholomew’s Hospital in London. They had conducted a follow-up of all cases of breast cancer treated at their institution in the 1930s by all methods of treatment and all surgeons; their cohort included patients receiving local radiation treatment

by Keynes as described earlier. No difference in survival was detected¹⁶.

In the United States, the greatest proponent for more conservative treatment was George Crile Jr. of the Cleveland Clinic¹⁷. Crile’s studies compared his patients having no clinical evidence of disease beyond the breast, on whom he had performed a simple mastectomy without axillary dissection and no radiotherapy, with patients who underwent radical mastectomy with other surgeons at the Cleveland Clinic. He found no difference in survival.

4. PETERS AND BREAST-CONSERVING SURGERY (LUMPECTOMY)

4.1 Early Observations

Peters was of course aware of the literature and had observed apparently good results in patients from her institution who had undergone conservative surgical procedures. She seized the opportunity to study the large group of patients in the records of the Princess Margaret Hospital, the successor to the old Radiotherapy Institute. Her first publication on the subject of conservative management appeared in 1967⁸. She reported retrospectively on more than 7000 patients who were seen between 1935 and 1960, of whom 852 had undergone excisional biopsy (wedge resection, lumpectomy), with 124 of those 852 having had no further treatment other than radiation. The remainder underwent either radiation and mastectomy, or mastectomy and radiation. There was no difference in 5-year survival between any of the three approaches. These patients were, of course, not part of a planned controlled study.

In 1968, Peters gave a talk at a National Cancer Conference in Denver, Colorado¹⁸, and in 1969, a similar invited address titled “The Role of Excisional Biopsy and Radiation in the Treatment of Early Breast Cancer” at the Annual Clinical Conference on Breast Cancer at the M.D. Anderson Hospital, Houston, Texas¹⁹. She spoke about stage I and II patients with breast cancer treated by local excision and radiation. She was conservative in her conclusions, but did suggest that “this [conservative] method of treatment appears to be equally as effective as other [radical] methods of treatment.” This view received little support from surgeons. Years later, she reflected, “I was refuted and shunned by most of the outstanding surgeons in the States—except for Dr. George Crile of Cleveland”⁹.

However, unbeknownst to Peters, there was one other surgeon who was impressed with her work. In the 1960s, the radiation oncologists at the M.D. Anderson Hospital in Houston, Texas, were interested in pursuing a more conservative approach to patients with early-stage breast cancer, and they invited Peters to speak on the subject at their conference (as earlier described). Of course, a conservative approach

required surgeons willing to collaborate. According to Dr. Eleanor Montague, a distinguished radiation oncologist at M.D. Anderson, the 1969 presentation by Peters in Houston convinced at least one surgeon. In Dr. Montague's words, "Vera was invited to our conference [November 1969]. It was enough to convince one of our surgeons"²⁰. Subsequently, excisional biopsy (lumpectomy) with postoperative radiation was initiated at the M.D. Anderson Hospital.

4.2 Skepticism, Disbelief and Debate

Skepticism regarding conservative surgery continued. In 1979, Peters received a letter from a radiation oncologist in the Netherlands. The writer, a woman, reflected that, in the late 1960s, she referred to an article by Peters about lumpectomy and was severely criticized. She wrote "I was nearly killed for it"²¹.

The debate continued, but at least there was a debate. In July 1974, at the annual meeting of the Canadian Medical Association, Dr. Peters, Dr. Leo Mahoney (a Toronto breast surgeon), and others from Toronto suggested that, compared with radical surgery, conservative surgery appeared to result in no survival disadvantage. A distinguished visiting surgeon, Dr. Jerome Urban, from Memorial Sloan-Kettering Cancer Institute in New York City disagreed and claimed that breast cancer must be treated with extensive surgery²².

It should be emphasized that none of the studies dating to the late 1960s—the study by Peters included—had appropriate control groups. There were certainly no prospective randomized clinical trials and no studies with properly matched historical controls.

A 1972 publication criticized the reports from all proponents (including Peters, Mustakallio, and Crile) of conservative operations in breast cancer patients, arguing that the results were flawed because of selection bias and inadequate controls²³.

4.3 The Final Study

Peters was not prepared to give up. At that time, clinical epidemiology and the use of proper design were just entering the culture of clinical studies. Peters chose to undertake a retrospective case-control study. The case material was already available in the vast case records of the Princess Margaret Hospital. From among the 8000 patients with breast cancer who had been managed from 1939 to 1969, clinical stage I patients were selected, and of those patients, all who had local undergone excision and breast irradiation ($n = 217$) were the study patients. Each patient was matched—by age, size of tumour, and year treated—with a patient treated by radical or modified radical mastectomy and radiation ($n = 217$). Deletion of 72 pairs, which included all deaths from other than cancer within 10 years after treatment (from both the

study and the control groups), left a study population of 145 pairs. The large number of exclusions was a result of the number of elderly patients with cardiovascular disease selected by their surgeons for conservative surgery. Age having been a criterion for matching in the study, equal numbers of older patients were deleted from the study group and the control group alike. No statistical overall survival difference was detected between the two groups, although the conservatively treated study group had slightly better survival than the control (extensive surgery) group. In addition, the physical deformity resulting from the more radical procedures was eliminated in the study group.

Peters was invited to report her findings to a large surgical audience as the Surgical Lecturer at the 1975 Royal College of Physicians and Surgeons of Canada meeting in Winnipeg, Manitoba. Her physician daughter, who attended the meeting, reports that the talk was greeted with a degree of coolness and skepticism. That view was confirmed subsequently by surgeons of the time^{24,25}. The paper was published in the *Annals of the Royal College of Physicians and Surgeons of Canada*²⁶, which unfortunately did not have a large international circulation. Two years later, Peters published an updated version in an international journal²⁷. The conclusions regarding survival were the same as in her previous publication, but they reached a much larger audience. This latter publication had particular historical significance because Peters retired in 1976, and it was the culmination of her work on early breast cancer. She made her final statement in the peer-reviewed literature: "As more and more conservative studies ripen, as more and more concerned physicians observe the adverse effects of excessive treatment, as more and more women become armed with knowledge, mastectomy, in early breast cancer, may become as old-fashioned as bloodletting."

5. CONFIRMATION

By the 1970s, the time had come for prospective randomized controlled trials to establish once and for all the role of breast-conserving surgery. In 1973, planning for a prospective randomized study began at the Princess Margaret Hospital in Toronto²⁸; that study, however, did not get off the ground.

At about the same time, planning also started for the large prospective randomized trial under the auspices of the National Surgical Adjuvant Breast and Bowel Project (NSABP). The NSABP trial B.06 began entry of patients in 1976, one year after Peters first reported her retrospective case-control study. The B.06 study prospectively randomized more than 2000 individuals with stage I or II breast cancer. It compared lumpectomy with and without radiation to the breast with total mastectomy without radiation. The 20-year follow-up of the NSABP study was reported in 2002 and established that there was no significant difference

in disease-free or overall survival between any of the three groups. There was, however, a significant decrease in local recurrence of tumour in the breast for those patients who had lumpectomy followed by radiation as compared with patients who had lumpectomy without radiation²⁹. Thus, lumpectomy followed by radiation became the standard treatment for patients with early-stage breast cancer. Simultaneously, a report emerged of a 20-year follow-up of an Italian randomized study of 701 women with stage I breast cancer. Radical mastectomy was compared with quadrantectomy followed by radiation. The long-term survival rate was the same in both groups³⁰. Peters's work and the value of breast-conserving surgery had finally been confirmed.

6. DISCUSSION AND SUMMARY

Peters was not the first person to suggest something less than radical mastectomy. A number of individuals in Europe, the British Isles, and the United States^{11,13,14,16,17} had been proponents of more local treatment. None had carried out appropriate controlled studies.

The evolution of Peters's thinking began when she observed the large number of post-radical mastectomy surgical patients referred to the Toronto radiotherapy facility. These patients had a profound impact on her. She became concerned about the physical and psychological effect that radical mastectomy had on the patients. Her subsequent favourable observations concerning patients who, for a variety of reasons, had been surgically treated by removal of the tumour only, prompted her to finally undertake her retrospective case-control study: a comparison that found no difference in survival between patients with stage I cancer of the breast treated with lumpectomy followed by radiation and those treated with radical or modified radical mastectomy followed by radiation^{26,27}. Hers was the first satisfactorily designed controlled study—albeit retrospective one—to address the issue. Over the subsequent 10–20 years, two large prospective randomized controlled studies^{29,30} confirmed her conclusions.

Peters, throughout her career, had a catholic interest in patients with breast cancer, including all stages and clinical aspects of the disease. However, it was her contributions to the conservative management of early-stage breast cancer that attracted international attention and, together with her work in patients with Hodgkin disease, resulted in international acclaim. She received numerous awards and honours, including prestigious medals from Europe and the United States^a. At home her accolades included honorary

degrees and the Order of Canada; she first became a Member and later an Officer of the Order for her internationally recognized contribution to research on breast cancer and Hodgkin disease.

In the words of Eleanor Montague, the well-known and highly respected oncologist from the M.D. Anderson Hospital in Texas, "Peters' [work] was ground-breaking in treating patients with early breast cancer"²⁰.

There is no doubt that the quiet, determined, single-minded career-long approach of Vera Peters played a major role locally, nationally, and internationally in steering toward an alternative—and now accepted—conservative and much more acceptable treatment for women with early-stage breast cancer.

7. ACKNOWLEDGMENTS

My thanks go to Cancer Care Ontario for support; to Drs. Kathleen Pritchard, John C. Laidlaw, and Anca Prica for reviewing this document and for their valuable advice; and to Ms. Luanne MacKenzie for typing and technical help.

8. REFERENCES

1. Cowan DH. Vera Peters and the curability of Hodgkin disease. *Curr Oncol* 2008;15:206–10.
2. Kalne R. *The Illustrated History of Surgery*. 2nd ed. London, UK: Harold Starke Publishers; 2000: 233–5.
3. Halsted WS. I. A clinical and histological study of certain adenocarcinomata of the breast: and a brief consideration of the supraclavicular operation and of the results of operations for cancer of the breast from 1889 to 1898 at the Johns Hopkins Hospital. *Ann Surg* 1898;28:557–76.
4. Ontario Medical Association Archives, Oral History Collection. Interview with Dr. Vera Peters. November 1979.
5. Annual Reports of the Ontario Radiotherapy Institute. Toronto: Ontario Institute of Radiotherapy; 1934–1941. [Available from: University Health Network archives; Ontario Cancer Institute/Princess Margaret Hospital fonds 940012, Box 1, 2.93–2.100]
6. MacKay EN, Sellers AH. Breast cancer at the Ontario cancer clinics, 1938–1956: a statistical review. *Can Med Assoc J* 1965;92:647–51.
7. Richards GE. Mammary cancer; the place of surgery and of radiotherapy in its management. *Br J Radiol* 1948;2:109–27.
8. Peters MV. Wedge resection and irradiation. An effective treatment in early breast cancer. *JAMA* 1967;200:134–5.
9. Peters MV. Address to the Oakville Medical Society [manuscript]. n.d. [Probably early 1980s] [Available from: University of Toronto Archives 19960019, Box 1001]
10. Peters MV. Carcinoma of the breast with particular reference to preoperative radiation. *J Can Assoc Radiol* 1953;4:32–9.
11. McWhirter R. The value of simple mastectomy and radiotherapy in the treatment of cancer of the breast. *Br J Radiol* 1948;21:599–610.
12. Peters MV. Note [manuscript]. n.d. [Available from: University of Toronto Archives 19960019, Box 1001]

^a La Médaille du Centre Antoine Béchère, Centre de relations internationales en radiologie médicale (Paris, France), 1977; and the Gold Medal Award, American Society of Therapeutic Radiology and Oncology, 1979.

13. Keynes J. Conservative treatment of carcinoma of the breast. *Br Med J* 1937;2:643–7.
14. Mustakallio S. Treatment of breast cancer by extirpation and radiation. *J Fac Radiol* 1954;6:23–5.
15. Smithers DW. Cancer of the breast: a study of short survival in early cases and of long survival in advanced cases. *Am J Roentgenol Radium Ther Nucl Med* 1958;80:740–58.
16. Porritt A. Early carcinoma of the breast. *Br J Surg* 1964;51:214–16.
17. Crile G Jr. Results of simple mastectomy without irradiation and the treatment of operative stage I cancer of the breast. *Ann Surg* 1967;168:144–5.
18. Peters MV. Presentation on the treatment of breast cancer. In: Proceedings of the Sixth National Cancer Conference; Denver, Colorado; September 18–20, 1968. Philadelphia, PA: J.P. Lipincott; 1970: 163–71.
19. Peters MV. The role of excisional biopsy and radiation in the treatment of early breast cancer. Presented at the 14th Annual Clinical Conference on Cancer; The University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, TX; November 6–7, 1969. [Available from: University of Toronto Archives 19960019, Box 1002]
20. Dr. Eleanor Montague. Interview with author. November 2006.
21. Letter to Peters from Prof. Dr. Brigit van der Werf-Messing, Rotterdam Radiotherapy Institute, February 1979. Family files.
22. Dunlop M. Breast removal questioned. *Toronto Star* June 29, 1974: A5. [Available from: University of Toronto Archives, Peters clipping file]
23. Anglem TJ, Leber RE. The dubious case for conservative operation in operable cancer of the breast. *Ann Surg* 1972;176:625–32.
24. Dr. William Spence. Interview with author. July 27, 2006.
25. Dr. Edward Fish. Interview with author. June 29, 2006.
26. Peters MV. Cutting the “Gordian knot” in early breast cancer. *Ann R Coll Physicians Surg Can* 1975;8:186–92.
27. Peters MV. Wedge resection with or without radiation in early breast cancer. *Int J Radiat Oncol Biol Phys* 1977;2:1151–6.
28. Cancer of the breast. In: *Annual Report: The Ontario Cancer Institute incorporating Princess Margaret Hospital* [Department of Medicine section]. Toronto: Ontario Cancer Institute incorporating Princess Margaret Hospital; 1973.
29. Fisher B, Anderson S, Bryant J, *et al*. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–41.
30. Veronesi U, Cascinelli N, Mariani L, *et al*. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;347:1227–32.

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