

# SURGICAL ONCOLOGY

A review journal of cancer management and research

August 1994, Volume 3, Issue 4, Pages 211–219

Natural immunity in breast cancer patients during neoadjuvant chemotherapy and after surgery

P. Beitsch, E. Lotzová†, G. Hortobagyi, R. Pollock

University of Texas, M.D. Anderson Cancer Center, Houston, TX 77030, USA

†Recently deceased.

## Abstract

Breast cancer is the most common cancer in women. Surgery, and more recently neoadjuvant chemotherapy, are being utilized as the initial treatment for breast cancer; however little is known about their effects on the natural immune system. The natural immune system (natural killer [NK] cells) is thought to be important in immune surveillance, including protection from metastasis during the intravascular tumour seeding that occurs during surgery.

To investigate the effects of surgery on the natural immune system, we studied the pre-operative and post-operative peripheral blood lymphocytes (PBL) of 10 patients with stage I or II breast cancer: there was a  $71.6 \pm 25.3\%$  post-operative reduction in NK cell function ( $P < 0.005$ , Student's paired *t*-test). To investigate the effects of neoadjuvant chemotherapy and surgery, we examined PBL from five patients with stage III breast cancer: NK cell function dropped  $95.7 \pm 1.9\%$  after neoadjuvant chemotherapy, and there was a further  $51.0 \pm 23.4\%$  decrease after surgery ( $P < 0.05$ , Student's paired *t*-test). Neither group of patients had decreased numbers of NK cells, changes in the percentage of T helper or suppressor cells, or alterations in the production of cytotoxic factor by NK cells. These findings suggest that the impairment in NK cell function reflects a defect in the ability of NK cells to recognize and/or bind to tumour target cells.

We conclude that the initial treatment of breast cancer patients, whether it involves surgery alone or with neoadjuvant chemotherapy, profoundly impairs their natural immune system and could increase the risk of metastasis. Further studies are needed to delineate the mechanism of this derangement in natural immunity and possibly alter its course.

## References

1. Boring, CC, Squires, TS, Tong, T, Montgomery, S. Cancer statistics, 1994. CA Cancer J Clin. 1994;44:7–26.
  - [CrossRef](#)

- | [PubMed](#)
2. Harris, JR, Morrow, M, Bonadonna, G. Cancer of the breast. in: VT DeVita, S Hellman, SA Rosenberg (Eds.) *Cancer: Principles & Practice of Oncology*. 4th edn. JB Lippincott Co, Philadelphia; 1993:1264–1332.
  3. Hanna, N. Role of natural killer cells in control of cancer metastasis. *Cancer Metastasis Rev*. 1982;1:45–64.
    - [CrossRef](#)
    - | [PubMed](#)
    - | [Scopus \(69\)](#)
  4. Barlozzari, T, Leonhardt, J, Wiltrout, RH, Herberman, RB, Reynolds, CW. Direct evidence for the role of LGL in the inhibition of experimental tumour metastases. *J Immunol*. 1985;134:2783–2789.
    - [PubMed](#)
  5. Uchida, A, Yanagawa, E. Natural killer cell activity and autologous tumour killing activity in cancer patients: overlapping involvement of effector cells as determined in two-target conjugate cytotoxicity assay. *J Natl Cancer Inst*. 1984;73:1093–1100.
    - [PubMed](#)
  6. Pollock, RE, Babcock, GF, Romsdahl, MM, Nishioka, K. Surgical stress-mediated suppression of murine natural killer cell cytotoxicity. *Cancer Res*. 1984;44:3888–3891.
    - [PubMed](#)
  7. Pollock, RE, Lotzova, E. Surgical-stress-related suppression of natural killer cell activity: a possible role in tumour metastasis. *Nat Immun Cell Growth Regul*. 1987;6:269–287.
    - [PubMed](#)
  8. Pollock, RE, Lotzova, E, Stanford, SD. Surgical stress impairment of murine natural killer cell cytotoxicity involves pre- and post-binding events. *J Immunol*. 1989;143:3396.
    - [PubMed](#)
  9. Pollock, RE, Stanford, S, Lotzova, E. Long-term murine natural killer cell recycling is impaired by surgical stress. in: *Surg Forum*. 39. 3rd edn. ; 1988:423–424.
  10. Guillou, PJ, Hegarty, J, Ramsden, C et al, Changes in human natural killer activity early and late after renal transplantation using conventional immunosuppression. *Transplant*. 1982;33:414–442.
    - [CrossRef](#)
    - | [PubMed](#)
  11. Tonnesen, E, Mickley, H, Grunnet, N. Natural killer cell activity during premedication, anaesthesia and surgery. *Acta Anaesthesiol Scand*. 1983;27:238–241.
    - [CrossRef](#)
    - | [PubMed](#)
  12. Ryhanen, P, Huttunen, K, Ilonen, J. Natural killer cell activity after open-heart surgery. *Acta Anaesthesiol Scand*. 1984;28:490–492.
    - [CrossRef](#)
    - | [PubMed](#)
  13. Buinauskas, P, McDonald, GO, Cole, WH. Role of operative stress on the resistance of the experimental animal to inoculated cancer cells. *Ann Surg*. 1958;148:642–648.
    - [CrossRef](#)
    - | [PubMed](#)
  14. Cunningham-Rundles, S, Fillipa, DA, Braun, DW, Antonelli, P, Ashikari, H. Natural cytotoxicity of peripheral blood lymphocytes and regional lymph node cells in breast cancer in women. *J Natl Cancer Inst*. 1981;67:585–590.
    - [PubMed](#)
  15. White, D, Jones, DB, Cooke, T, Kirkham, N. Natural killer activity in peripheral blood lymphocytes of patients with benign and malignant disease. *Br J Cancer*. 1982;46:611–616.

- [CrossRef](#)
  - | [PubMed](#)
16. Garner, WL, Minton, JP, James, AG, Hiffman, CC. Human breast cancer and impaired NK cell function. *J Surg Oncol.* 1983;24:64–66.
- [CrossRef](#)
  - | [PubMed](#)
17. Robinson, E, Rubin, D, Mekori, T, Segal, R, Pollack, S. *In vivo* modulation of natural killer cell activity by tamoxifen in patients with bilateral primary breast cancer. *Cancer Immunol Immunother.* 1993;37:209–212.
- [CrossRef](#)
  - | [PubMed](#)
  - | [Scopus \(21\)](#)
18. Cannon, GB, Bonnard, GD, Djeu, J, West, WH, Herbertman, RB. Relationship of human natural lymphocyt-mediated cytotoxicity of breast cancer-derived target cells. *Int J Cancer.* 1977;19:487–497.
- [CrossRef](#)
  - | [PubMed](#)
19. Eremin, O, Coombs, RRA, Ashby, J. Lymphocytes infiltrating human breast cancers lack K-cell activity and show low levels of NK-cell activity. *Br J Cancer.* 1981;44:166–175.
- [CrossRef](#)
  - | [PubMed](#)
20. Heidenreich, W, Jagla, K, Schussler, J et al, Spontaneous cell-mediated cytotoxicity (SCMC) and anti-body-dependent cellular cytotoxicity (ADCC) in peripheral blood and draining lymph nodes of patients with mammary carcinoma. *Cancer Immunol Immunother.* 1979;7:65–69.
- [CrossRef](#)
  - | [Scopus \(7\)](#)
21. Miyazaki, S, Akiyoshi, T, Arinaga, S et al, Depression of the generation of cell-mediated cytotoxicity after surgery. *Jap J Surg.* 1983;13:191–195.
- [CrossRef](#)
  - | [PubMed](#)
  - | [Scopus \(2\)](#)
22. Lukomska, B, Olszewski, WL, Engeset, A et al, The effect of surgery and chemotherapy on blood NK cell activity in patients with ovarian cancer. *Cancer.* 1983;51:465–469.
- [CrossRef](#)
  - | [PubMed](#)
23. Schantz, SP, Romsdahl, MM, Babcock, GF et al, The effect of surgery on natural killer cell activity in head and neck cancer patients: in vitro reversal of a postoperatively suppressed immunosurveillance system. *Laryngoscope.* 1985;95:588–594.
- [CrossRef](#)
  - | [PubMed](#)
24. Uchida, A, Kold, R, Micksche, M. Generation of suppressor cells for natural killer activity in cancer patients after surgery. *J Natl Cancer Inst.* 1982;68:735–741.
- [PubMed](#)
25. Pollock, RE, Lotzová, E, Stanford, SD. Surgical stress impairs natural killer cell programming of tumour for lysis in patients with sarcomas and other solid tumours. *Cancer.* 1992;70:2192–2202.
- [CrossRef](#)
  - | [PubMed](#)
  - | [Scopus \(74\)](#)

26. Sewell, HF, Halbert, CF, Robins, RA et al, Chemotherapy-induced differential changes in lymphocyte subsets and natural-killer-cell function in patients with advanced breast cancer. *Int J Cancer*. 1993;55:735–738.
- [CrossRef](#)
  - | [PubMed](#)
  - | [Scopus \(36\)](#)
27. Brenner, BG, Margoese, RG. The relationship of chemotherapeutic and endocrine intervention on natural killer cell activity in human breast cancer. *Cancer*. 1991;68:482–488.
- [CrossRef](#)
  - | [PubMed](#)
28. Valavaara, R, Tuominen, J, Toivanen, A. The immunological status of breast cancer patients during treatment with a new antiestrogen, toremifene. *Cancer Immunol Immunother*. 1990;31:381–386.
- [CrossRef](#)
  - | [PubMed](#)
  - | [Scopus \(12\)](#)
29. Roberts, S, Long, L, Johansson, O, McGrath, R, McGrew, E, Cole, WH. The isolation of cancer cells from the blood stream during uterine curettage. *Surg Gynecol Obstet*. 1960;3:3–11.
30. Liotta, LA, Saidel, MG, Kleinerman, J. The significance of hematogenous tumour cell clumps in the metastatic process. *Cancer Res*. 1976;36:889–894.
- [PubMed](#)