

Surgery for cancer in the elderly: state of the art

B. AMATO¹, L. SIVERO¹, G. VIGLIOTTI¹, C. RISPOLI², N. ROCCO¹, L. IANNONE¹
S. TESTA¹, V. SALVATI¹, R. COMPAGNA¹, M. GENTILE¹, M. DONISI¹

The elderly present generally more extensive and advanced cancer. Once the diagnosis of cancer has been placed in the elderly, the decision of the treatment would seem to be correlated with the age. The literature suggests that cancer surgery patients older than 80 years, who underwent surgery or radiation therapy, have worse outcomes when compared with young patients with similar cancer. However, analysis derived from more recent studies consider the age as an independent risk factor, including the chronological age only in the pre-operative risk factors.

KEY WORDS: Neoplasms - Aged - Surgical procedures, operative.

Cancer is an increasingly common lifetime event, occurring approximately 10 times more frequently in the elderly than in younger patients due in large part to a rising life expectancy in the most privileged parts of the world, currently greater than 80 years in much of Europe, North America, Australia, and New Zealand.¹⁻⁴

A clear definition of "elderly" is rather difficult to formulate, as physiologic age becomes recognized as more relevant than chronological age. Nevertheless, studies must use a cut-off value, such as 65 years^{2,3} and 85 years,⁴ to define the older population at higher risk of developing cancer. For those who survive to old age, the lifetime risk of developing any invasive cancer is higher for men (44%) than women (38%).⁴

Despite the growing emphasis on physiologic age versus chronological age in the assessment of an individual's risk/benefit ratio dealing with cancer surgery, there are several issues relevant to the elderly population (as identified by chronological age) as they face increasing rates of cancer. These issues include but are not limited to the underrepresentation of elderly patients in randomized clinical trials,⁵⁻⁷ the impact of social connections on risk in the elderly,⁸ the changing risk/benefit ratio associated with cancer screening, ageism among professional health providers, the possibility of increased risk of perioperative morbidity and mortality following cancer surgery and the physiologic changes associated with aging and impacting the ability of

¹Department of General, Geriatric Oncologic Surgery and Advanced Technologies "Federico II" University of Naples, Naples, Italy

²Department of General and Emergency Surgery ASL Napoli1 Centro, Naples, Italy

oncogeriatric patients to avoid cancer and to recover from cancer surgery.

Ageism, or prejudice based on age alone, may be present when older patients come for evaluation of a cancer and are evaluated for their diagnosis and offered treatment recommendations. As one ages, a progressive but largely variable loss of physiological and cognitive function occurs and is relevant to the evaluation of an elderly cancer patient.¹⁰⁻¹³ Due to this loss of function, along with increasing comorbidities, a more comprehensive assessment of the geriatric patient may be warranted.

Once the diagnosis of cancer has been made in an elderly individual, whether by screening or by investigation of symptoms, treatment decisions have been shown to correlate with chronologic age.

In a large survey of primary care providers in France, for instance, in a multi-variate analysis, chronological age of the patient was highly associated with the decision not to refer patients with advanced (not defined) cancer to oncologic specialties (odds ratio 0.55; 95% confidence interval 0.35-0.86; P=0.009).¹⁴

If elderly patients are referred to an oncologic specialty, further ageism may exist there too: in a survey of 1408 French medical and radiation oncologists to whom breast cancer patients were referred, significant differences in treatment choice were observed depending only on patient age.¹⁵

Following the 1990's National Institutes of Health Consensus Conference recommendation that patients with stage III colorectal cancer receive adjuvant chemotherapy to increase survival,¹⁶ 85934 patients were entered into the National Cancer Data Base and studied to determine whether adjuvant therapy failed to benefit any specific sets of patients; although elderly patients derived the same benefit as younger patients, they were less frequently treated.¹⁷

Corresponding author: Prof. B. Amato MD, Department of General, Geriatric, Oncologic Surgery and Advanced Technologies, "Federico II" University of Naples, Via Pansini 5, 80131 Naples, Italy.
E-mail: bramato@unina.it

Studies of cancer surgery in elderly patients

Once the decision has been made to proceed with a curative intent operation in an elderly patient, do operative outcomes support the decision to have elderly patients subjected to invasive procedures? Given that the greatest risks are associated with the largest operations,¹⁸ review of major thoracic and abdominal operations will prove most useful to answer this question.

In the thoracic surgical oncology literature, some large population-based studies, such as that by Owonikoko *et al.* analyzing the Surveillance, Epidemiology, and End Results (SEER) Database, including over 45000 patients, have suggested that patients >80 years old were less likely to undergo operation or radiation and had inferior outcomes when compared with younger patients.¹⁹ However, analysis of more recent studies focusing on age as an independent risk factor support the decreasing importance of chronological age alone in the preoperative risk evaluation of patients prior to esophageal^{20,21} and pulmonary²²⁻²⁵ resection.

Similarly, although large population-based studies in the pancreatic literature suggest worse short-term outcomes in older, compared to younger, patients,^{26,27} it is likely that "age" in these population-based studies was simply a surrogate for chronic illness. When large series of elderly patients undergoing major pancreatic and hepato-biliary operations are analyzed, chronological age turns out not to be a meaningful risk factor, although all agree that physiologic age as described above is essential to consider.²⁸⁻³⁴

Leaving aside the question of differences in the outcomes of morbidity and mortality in older versus younger patients, there are clearly other differences. For example, differences in histology exist in the elderly: an analysis of elderly lung cancer patients in the SEER database revealed fewer cases of adenocarcinoma in older patients: 33% in those <70 years old compared with 27% in those aged 70 to 79 years and 23% in patients ≥80 years old.²⁰ Even more relevant to the surgical treatment of elderly cancer patients is a study of the National Cancer Data Base (NCDB), including 142,009 NOMO patients who underwent colectomy for adenocarcinoma: adequate (≥12 nodes harvested) lymph node counts obtained in only 41% if patients >78 years old (median 10 nodes) compared to 48% in patients <67 years old (median 11 nodes). Given that one of the key prognostic indicators of colorectal cancer is the number of lymph nodes harvested during surgical resection, this study highlights the need for increased use of techniques to increase the harvest in elderly patients.

Increased awareness of such age-related differences is mandatory for those providing surgical treatment for the increasing elderly population of cancer patients.

Riassunto

Chirurgia per tumori nel paziente anziano: stato dell'arte

Gli anziani presentano generalmente neoplasie più estese ed avanzate. Una volta che la diagnosi di tumore è stata posta in anziani, la decisione del trattamento sembra essere correlata con l'età anagrafica. La letteratura oncologica della chirurgia suggerisce che pazienti con più di 80 anni, sottoposti a intervento chirurgico o terapia radiante, hanno risultati peggiori se confrontati con pazienti gio-

vani, affetti da neoplasie simili. Tuttavia analisi derivate da studi più recenti, considerano l'età un fattore di rischio indipendente, considerando l'età anagrafica solo nei fattori di rischio pre-operatorio.

PAROLE CHIAVE: Tumori - Età avanzata - Trattamento chirurgico.

References

1. WorldBank, "Life Expectancy," 2011, <http://data.worldbank.org/data-catalog/world-development-indicators?cid=GPD.WDI>.
2. Yancik R. Cancer burden in the aged: an epidemiologic and demographic overview. *Cancer* 1997;80:1273-83.
3. Yancik R. Epidemiology of cancer in the elderly. Current status and projections for the future. *Int J Radiol Sci* 1997;22:3-9.
4. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clinicians* 2010;60:277-300.
5. Lang KJ, Lidder S. Under-representation of the elderly in cancer clinical trials. *Br J Hospital Med* 2010;71:678-81.
6. Al-Refaie WB, Habermann EB, Dudeja V *et al.* Extremity soft tissue sarcoma care in the elderly: insights into the generalizability of NCI cancer trials. *Ann Surg Oncol* 2010;17:1732-8.
7. Dudeja V, Habermann EB, Zhong W *et al.* Guideline recommended gastric cancer care in the elderly: insights into the applicability of cancer trials to real world. *Ann Surg Oncol* 2010;18:26-33.
8. Liu L, Newschaffer CJ. Impact of social connections on risk of heart disease, cancer, and all-cause mortality among elderly Americans: findings from the second longitudinal study of aging (LSOA II). *Arch Gerontol Geriatr* 2011;53:168-73.
9. Du XL, Fang S, Meyer TE. Impact of treatment and socioeconomic status on racial disparities in survival among older women with breast cancer. *Am J Clin Oncol* 2008;31:125-32.
10. Ramesh HS, Boase T, Audisio RA. Risk assessment for cancer surgery in elderly patients. *Clin Interv in Aging* 2006;1:221-7.
11. Ramesh SH, Jain S, Audisio RA. Implications of aging in surgical oncology. *Cancer J* 2005;116:488-94.
12. Audisio RA, Ramesh H, Longo WE, Zbar AP, Pope D. Preoperative assessment of surgical risk in oncogeriatric patients. *Oncologist* 2005;104:262-8.
13. Crivellari D, Fratino L. Special populations: elderly patients. *Cancer Treat Res* 2009;151:299-315.
14. Stuck AE, Aronow HU, Steiner A *et al.* A trial of annual in-home comprehensive geriatric assessments for elderly people living in the community. *New Engl J Med* 1995;333:1184-9.
15. Delva F, Marien E, Fonck M *et al.* Factors influencing general practitioners in the referral of elderly cancer patients. *BMC Cancer* 2011;11:5.
16. Protière C, Viens P, Rousseau F, Moatti JP. Prescribers' attitudes toward elderly breast cancer patients. *Discrimination or empathy?* *Crit Rev Oncol Hematol* 2010;752:138-50.
17. NIH-CRC-Consensus, NIH consensus conference. Adjuvant therapy for patients with colon and rectal cancer. *JAMA* 1990;264:1444-50.
18. Jessup JM, Stewart A, Greene FL, Minsky BD. Adjuvant chemotherapy for stage III colon cancer: implications of race/ethnicity, age, and differentiation. *JAMA* 2005;294:2127-33.
19. Owonikoko TK, Ragin CC, Belani CP *et al.* Lung cancer in elderly patients: an analysis of the surveillance, epidemiology, and end results database. *J Clin Oncol* 2007;25:5570-7.
20. Honor C, Al-Azzeh A, Gilson N *et al.* Esophageal cancer surgery in patients older than 75: long term results. *Acta Chirurgica Belgica* 2011;111:12-7.
21. Jougon JB, Ballester M, Duffy J *et al.* Esophagectomy for cancer in the patient aged 70 years and older. *Ann Thor Surg* 1997;63:1423-7.
22. Bolukbas S, Eberlein MH, Schirren J. Pneumonectomy vs. sleeve resection for non-small cell lung carcinoma in the elderly: analysis of short-term and long-term results. *Thorac Cardiovasc Surg* 2011;59:142-7.
23. Rivera C, Falcoz PE, Bernard A, Thomas PA, Dahan M. Surgical management and outcomes of elderly patients with early stage non-small cell lung cancer: a nested case-control study. *Chest* 2011;140:874-80.
24. Zuin A, Marulli G, Breda C *et al.* Pneumonectomy for lung cancer over the age of 75 years: is it worthwhile? *Interact Cardiovasc Thorac Surg* 2010;106:931-5.

25. Rivera C, Dahan M, Bernard A, Falcoz PE, Thomas P. Surgical treatment of lung cancer in the octogenarians: results of a nationwide audit. *Eur J Cardio-thorac Surg* 2011;396:981-6.
26. Riall TS, Reddy DM, Nealon WH., Goodwin JS. The effect of age on short-term outcomes after pancreatic resection: a population-based study. *Ann Surg* 2008;248:459-65.
27. Finlayson E, Fan Z, Birkmeyer JD. Outcomes in octogenarians undergoing high-risk cancer operation: a national study. *J Am Coll Surg* 2007;2056:729-34.
28. Makary MA, Winter JM, Cameron JL *et al.* Pancreatico-duodenectomy in the very elderly. *J Gastrointest Surg* 2006;10:347-56.
29. Petrowsky H, Clavien PA. Should we deny surgery for malignant hepato-pancreatico-biliary tumors to elderly patients? *World J Surg* 2005;299:1093-100.
30. di Sebastiano P, Festa L, Buchler MW, di Mola FF. Surgical aspects in management of hepato-pancreatico-biliary tumours in the elderly. *Best Practice Res Clin Gastroenterol* 2009;236:919-23.
31. Cannon RM, Martin RCG, Callender GG, Mcmasters KM, Scoggins CR. Safety and efficacy of hepatectomy for colorectal metastases in the elderly. *J Surg Oncol* 2011;1047:804-8.
32. Kulik U, Framke T, Grohennig A *et al.* Liver resection of colorectal liver metastases in elderly patients. *World J Surg* 2011;359:2063-72.
33. Rispoli C, Rocco N, Iannone L, Compagna R, Cacciapuoti MT, Bellino A, Amato B., Breast reconstruction in older women: a growing request. *BMC Ger* 2009;9S1:28.
34. Guida F, Antonino A, Conte P, Formisano G, Esposito D, Bencivenga M *et al.* Gastric cancer in elderly: clinico-pathological features and surgical treatment. *BMC Geriatrics* 2009;9S1:38.

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Received on October 15, 2012.

Accepted for publication on November 11, 2013.

MINERVA MEDICA
COPYRIGHT®