

LIVER RESECTION IN ELDERLY PATIENTS

Hepatectomia em pacientes idosos

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HEADINGS - Aged. Hepatectomy. Postoperative complications. Morbidity. Mortality.

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ABSTRACT - Introduction - Life expectancy of the population has increased in recent years as a result of human development, leading to an increase in the incidence of primary and secondary neoplasms of the liver. Medicine has been following this process, but there is still fear of aggressive surgical treatment in elderly patients, especially concerning to liver surgery. **Aim** - To analyze the influence of age on the morbidity and mortality of patients undergoing liver resection. **Method** - Literature review of scientific articles available in PubMed, Scielo and Bireme database with "elderly", "hepatectomy," "hepatic resection," "postoperative complications", "morbidity", "mortality". It was selected studies that compared the results of hepatectomy between groups of young and elderly patients. **Conclusion** - Age is not a predisposing factor for the worsening of results in liver resection.

RESUMO - Introdução - A expectativa de vida da população tem aumentado nos últimos anos, como também houve progressão da incidência de neoplasias primárias e secundárias do fígado. A medicina vem acompanhando esse processo, mas ainda há receios quanto ao uso de tratamentos cirúrgicos agressivos em pacientes idosos, especialmente no que tange à cirurgia do fígado. **Objetivo** - Analisar a influência da idade na morbimortalidade de pacientes submetidos à ressecção hepática. **Métodos** - Revisão bibliográfica através dos sites do PubMed, Scielo e Bireme, com os descritores "elderly", "hepatectomy", "hepatic resection", "postoperative complications", "morbidity", "mortality". Foram selecionados os trabalhos que compararam os resultados de hepatectomia entre grupos de pacientes jovens e idosos. **Conclusão** - A idade não é fator predisponente à piora dos resultados na ressecção hepática.

INTRODUCTION

Life expectancy worldwide has increased greatly in recent decades, causing aging population. This process is due to several factors such as the increase in the fertility rate prevalent in the past compared to the present, reducing child mortality, implementation of government policies to support the elderly, improvements in working conditions, access to public health services and best quality of life. Also contributes to this picture the improvement of social conditions and incessant development of technological and medical knowledge.

The Brazilian Institute of Geography and Statistics showed population growth which changed the pyramid age and Brazil, leading to important social, political and sanitary changes². Senescence, by itself, results in the onset of chronic diseases that can affect the quality and functionality in life in the elderly. For example, they are more often candidates for surgical procedures, either in emergency or elective.

With an aging population, according to the National Cancer Institute, the Program EUROCARE-3 and International Society for Geriatric Oncology, the prevalence of cancer reaches endemic proportions, with about half of cancers diagnosed in elderly patients^{3,4,5}

Within the context of cancer treatment, liver resection is the treatment

of choice for many primary and secondary diseases of the liver. Most studies in the elderly undergoing this procedure reported resection of primary and secondary liver tumors, especially hepatocellular carcinoma and colorectal metastatic cancer⁶. However, it was observed in the last two decades that hepatectomy became secure and also performed in the older population, implying paradigm shift in the approach of these patients⁷.

This paper intends to provide information on hepatectomy in elderly patients with the goal of surgical decision evaluating morbidity and improvement in quality of life in this age group.

METHOD

Literature review was conducted through the websites of PubMed, SciELO and Bireme with the keywords "elderly", "hepatectomy", "hepatic resection", "postoperative complications", "morbidity", "mortality". Were selected studies that compared the results of hepatectomy between young and elderly patients.

Hepatobiliary tumors

Hepatobiliary malignancies have their peak incidence between the sixth and eighth decades of life, most prevalent over 65 years⁸.

Surgical resection is the only potentially curative treatment for most primary and secondary hepatobiliary malignancies, when resectable and limited. Moreover, population aging, associated with the peak incidence of primary and secondary malignant tumors of the liver in the age group 65-85 years, has resulted in dramatic increase in the number of elderly patients undergoing liver resection. Unfortunately, many doctors consider that old age is a contraindication to curative surgical treatment, both high risk and limited expectancy of life. Often, the operation is not offered on the basis that patients are not referred for hepatobiliary surgeons and thus suffer the consequences of inadequate treatment⁹.

One argument used improperly for the definition of inadequate treatment is the bias of age, with the justification that these patients have lower life expectancy compared to younger age⁹. However, life expectancy in Brazil, according to IBGE in 2008, to a person of 60 years of age is expected more 21.3 years. This argument alone can justify that elderly patients with hepatobiliary malignancies should have appropriate treatment while their disease is limited and the coexisting comorbidities are controlled.

Worldwide, approximately 427,000 people die from hepatocellular carcinoma (HCC); is the fourth leading cause of cancer death in the world¹⁰. The peak incidence around the sixth decade of life, combined with an aging population, results in an increase of the elderly population with HCC considered for liver resection. Justification, as observed in experimental

models, is that, with advancing age, there is more DNA damage by oxidative stress and action of carcinogenic agents, leading thus to the neoplastic changes¹¹.

In some series, it was found that more than half of patients with HCC has over 65 years of age, and of these, more than 80% suffer from cirrhosis. The observed survival of elderly patients is lower than that of younger patients, usually by the fact that these patients have their later diagnosis or are treated inadequately^{12,13}. However, when comparing the same stages in resected patients, survival is similar between groups, ranging between 18 and 76% in five years^{9,14}.

Among the predictors of worse survival in the elderly population, as well as in younger patients, is cirrhosis and Child classification B/C⁸. Another peculiarity that was observed in aged patients, is a higher rate of infection by the hepatitis C virus and low hepatitis B. Also, there is a higher proportion of women, suggesting different hepatocarcinogenesis in elder¹⁵.

For the treatment of HCC is the non-surgical treatment modalities, generally palliative, such as radiofrequency, alcoholism and quimioembolization¹⁶. Only transplantation and liver resection has curative intent. The surgery is restricted to patients with or without cirrhosis or cirrhosis with Child-Pugh A without portal hypertension. In Western countries it is less than 5% the recurrence rate after resection⁹.

Several studies have examined the outcome of hepatic resection in patients young and old. Even with older patients having more comorbidities, were not observed impact on the rates of postoperative complications in the overall analysis of the studies. Mortality data also vary in the literature, with higher rates of complications in studies of decades ago^{17,18,19,20} and lower in more recent ones, due to better technical quality and skills improvement of surgeons⁹. Several studies considered resection of HCC safe in elderly patients with controlled comorbidities^{1,9,21,22,23,24,25,26,27,28,29,30,31}.

Even with expected lower life expectancy in selected elderly patients the five-year survival after resection of HCC was 28-58%, equivalent to that of younger ones. These data justify extensive liver resection in patients of this age with CHC^{9,21,22,27,28,29,31}

Colorectal metastases

Approximately 437,000 people die each year from colorectal cancer in the world, placing it as the third leading cause of cancer death. About 80% of colorectal tumors are diagnosed in patients between 65 and 85 years old^{5,9}, but it is important to note that, even with the increasing prevalence of colorectal neoplasia in elderly patients, the survival rate in this age group has not grown, explained by the fact that older people underwent curative surgical treatment of the primary tumor and its metastases less frequently³³.

The liver is the organ most frequently affected by distant metastases of colorectal neoplasia. The synchronic types are present in about 20% and

metachronous colorectal cancer in approximately 20-50%^{4,34}. It is known that liver resection is the only cure therapeutic option for patients with isolated hepatic metastases^{9,34,35}. However, studies have shown that the rate of resection of liver metastases of colorectal tumors is 8 to 20% in patients with more age^{34,35,36,37}. This justification becomes valid, because when weighing them against the benefits of surgical resection of liver metastases against the potential risks of surgery, many doctors are still reluctant to indicate surgical treatment in the elderly. While this approach is not based on scientific evidence, it is likely that concerns about morbidity and postoperative mortality in the elderly may influence the decision of not to offer the operation to them³⁴.

Recent improvements in techniques of liver resection and the anesthetic interventions have greatly improved the results. The postoperative mortality has fallen in recent decades, and today, perioperative mortality varies between 0 and 11% for resections of colon and liver metastasis combined. Still, neoadjuvant chemotherapy is used with the intention of improving disease-free survival after hepatic resection, and also provide patients with unresectable initial operation with curative potential³⁴.

Resection of liver metastases of colorectal cancer in elderly patients has been shown to be safe, with similar mortality in the non-elderly and elderly^{1,7,35,38,39,40,41,42,43,44,45,46,47,48,49}.

The five-year survival after liver resection reported by several studies varied from 28 to 58%, with median survival 16-46 months, similar to younger patients. Several recent studies have revealed that age by itself is not a risk factor for the outcome. The findings suggest that individuals with liver metastasis from colorectal cancer benefit from the same degree as younger patients. Moreover, hepatic resection for metastatic colorectal tumor should be the preferred option in elderly patients with comorbidities controlled^{1,35,38,38,39,40,41,43,45,48,49}.

Tumors of the biliary hilum

The tumor of the biliary hilum (Klatskin tumor) is the most common cancer of the biliary tract. The peak incidence of the disease occurs in the seventh decade of life⁹. The natural history is reserved, with few reports of survivors after five years from the diagnosis⁵⁰. Although surgical treatment is difficult and unquestionable, it is limited to specialized centers where radical resection is the only potential chance of cure.

Due to the increasing proportion of elderly patients diagnosed with this tumor are important questions to be answered about the extent of resection that can be performed safely and if this treatment would increase survival. Unfortunately there is no adequate studies to assess these issues in relation to age. There are only two publications in the literature suggesting that the five-year survival and median survival is similar in

patients young and old. Despite the absence of other comparative studies of age, survival data of these two small studies showed that elderly patients may benefit from extensive liver resection as well as young people, since well selected^{51, 52}.

Other indications for hepatectomy

In the literature there are also series comparing resection of metastases from colorectal and other tumors, benign hepatic cysts, hemangiomas, focal nodular hyperplasia, hepatocellular adenoma and hepatolithiasis between young and elderly patients. It was ascertained that the endpoint following the procedure in terms of morbidity, mortality and survival is similar in young as compared to elderly^{7,10,41,53,54,55,56,57,58,59,60}. However, these data are inserted into larger papers where the frequency of hepatocellular carcinoma, hilar bile duct tumors and metastasis of colorectal neoplasms stand out; it is not possible to compare separately the results of surgery in these diseases in the elderly.

Security of hepatectomy

It was observed that with the hepatectomy was obtained mortality reduction in recent years. In 1970, it was 20%, and presently is less than 5%^{6,61}.

At the same time, there have been advances in perioperative care. There was an improvement in the selection and preoperative preparation of patients, advances in anesthetic and intensive care postoperatively. There was better understanding of hepatic segmental anatomy and innovations in devices for transection of the liver, surgical technique more refined and more accurate control of hemostasis. These facts have improved the safety of operations. Innovations have allowed the expansion and constant modification of the eligibility criteria for hepatectomy including patients with associated chronic liver disease, especially the elderly⁴⁵.

Several studies have shown that liver resections are increasingly performed in elderly patients, with encouraging results. However, comparative studies that specifically examine the role of age on the outcome of liver resection in young and elderly subjects are still uncommon in the literature in relationship to the growing number of procedures performed in elder⁷. Previous studies in Europe, North America and Asia have shown that there is safety in hepatectomy in elderly patients with morbidity and mortality ranging between 9- 52.5% and 0-11%, respectively.

CONCLUSION

Age did not influence morbidity, in-hospital mortality and survival of patients undergoing hepatectomy, since they are well selected. This procedure should be encouraged in older patients, due

to the increasing number of individuals candidates for surgical treatment of their liver diseases.

REFERENCES

1. Adam R, Frilling A, Elias D, et al. and the LiverMetSurvey Centres. Liver resection of colorectal metastases in elderly patients. *British Journal of Surgery* 2010; 97: 366–376
2. Aguiar, LRF, Nassif PAN, Ribas CAPM, Czczko NG, Ribas MM, Marinho-Júnio CH, Wendler E. Regeneração do fígado após hepatectomia parcial em ratos submetidos à hipertensão portal pós-hepática. *ABCD Arq Bras Cir Dig*. 24(2):144-151, 2011.
3. Aldrighetti L, Arru M, Caterini R, et al. Impact of advanced age on the outcome of liver resection. *World J Surg* 2003;27:1149- 1154
4. Bockhorn M, Sotiropoulos GC, Sgourakis G, et al. Major liver resections in the elderly: is an aggressive approach justified? *Int J Colorectal Dis* 2009;24:83–86
5. Brand MI, Saclarides Tj, Dobson HD. Liver resection for colorectal cancer: liver metastases in the aged. *Am Surg* 2000;66:412
6. Brunken C, Rogiers X, Malago M. Is resection of colorectal liver metastases still justified in very elderly patients. *Chirurg* 1998;69:1334
7. Caratozzolo E, Massani M, Recordare A, et al. Liver resection in elderly: comparative study between younger and older than 70 years patients. Outcomes and implications for therapy. *G Chir* 2007;28:419-424
8. Carino NL. Liver resection for colorectal liver metastases in older patients. *Critical Review in Oncology/Hematology* 2008;67:273-278
9. Ferrero A, Vigano L, Polastri R. Hepatectomy as treatment of choice for hepatocellular carcinoma in elderly cirrhotic patients. *World J Surg* 2005;29:1101- 1105
10. Fong Y, Fong Y, Blumgart LH, Fortner JG. Pancreatic or liver resection for malignancy is safe and effective for the elderly. *Ann Surg* 1995;222:426
11. Hanazaki K, Kajikawa S, Shimozaawa N. Hepatic resection for hepatocellular carcinoma in the elderly. *J Am Coll Surg* 2001;192:38
12. Instituto Nacional do Câncer. Site do INCA. Rio de Janeiro: INCA; 2011
13. Jansen PLM. Liver disease in the elderly. *Best Practice and Research Clinical Gastroenterology*, 2002;16:149-158
14. Mann CD, Neal CP, Pattenden CJ, et al. Major resection of hepatic colorectal liver metastases in elderly patients e an aggressive approach is justified. *EJSO* 2008;34:428-432
15. Menon KV, Mukhtar AA, Aldouri A, et al. Outcomes after major hepatectomy in elderly patients. *J Am Coll Surg* 2006;203:677-683
16. Papamichael D, Audisio R, Horiot JC, et al. Treatment of the elderly colorectal cancer patient: SIOG expert recommendations. *Annals of Oncology* 2009;20:5–16
17. Petrowsky H, Clavien PA. Should we deny surgery for malignant hepato-biliary tumors to elderly patients? *World J Surg* 2005;29:1093-1100
18. Pisani, P. Estimates of the worldwide mortality from 25 cancers in 1990. *Int J Cancer* 1999;83:18-29
19. Poon RT, Fan ST, Lo CM. Hepatocellular carcinoma in the elderly: results of surgical and nonsurgical management. *Am J Gastroenterol* 1999;94:2460
20. Portolani N, Baiocchi GL, Coniglio A, et al. Limited liver resection: a good indication for the treatment of hepatocellular carcinoma in elderly patients. *Jpn J Clin Oncol* 2011;41:1358-65
21. Quaglia A, Capocaccia R, Micheli A, et al and the EURO-CARE-3 Working Group. A wide difference in cancer survival between middle aged and elderly patients in Europe. *Int J Cancer* 2007;120:2196-2201
22. SEER Cancer Statistics Review 1975-2001, 2011.
23. Temple LK, Hsieh L, Wong WD. Use of surgery among elderly patients with stage IV colorectal cancer. *J Clin Oncol* 2004;22(17):3475-84
24. Wu CC, Chen JT, Ho WL et al. Liver resection for hepatocellular carcinoma in octogenarians. *Surgery* 1999;125:332
25. Yamamoto K, Takenaka K, Matsumata T, et al. Right hepatic lobectomy in elderly patients with hepatocellular carcinoma. *Hepatogastroenterology* 1997;44:514
26. Yeh CN, Lee WC, Jeng LB. Hepatic resection for hepatocellular carcinoma in elderly patients. *Hepatogastroenterology* 2004;51:219
27. Zieren HU, Muller JM, Zieren J. Resection of colorectal liver metastases in old patients. *Hepatogastroenterology* 1994;41:34