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THE ROLE OF HILAR LYMPHADENECTOMY IN PATIENTS SUBJECTED TO HEPATECTOMY DUE TO COLORECTAL METASTASIS

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ABSTRACT – ***Context*** - Hepatectomy is the treatment of choice for colorectal liver metastases, and several studies have shown good results, with 5-year survival rates ranging from 40% to 57%. Several clinical and pathological predictive factors for survival after liver resection have been studied. Involvement of the hepatic hilum lymph nodes, the incidence of which varies from 2% to 10%, indicates a poor long-term prognosis. ***Results*** - Despite variable results, some authors have reported a not-insignificant improvement in survival rate in liver-metastasis patients with hilar lymph node involvement who undergo combined liver resection and lymphadenectomy. Due to the low rates of morbidity and mortality for liver-resection surgery, several specialized centers perform liver resections combined with lymphadenectomies in selected cases. It should be noted that the therapeutic value of systemic lymphadenectomy is not yet entirely understood, and only controlled studies comparing groups with and without lymphadenectomy can fully resolve the issue. ***Conclusion*** - In any case, hilar lymph node dissection has been shown to be a useful tool for improving the accuracy of extra hepatic disease staging, regardless of its impact on survival.

HEADINGS – Neoplasm metastasis. Lymph node excision. Hepatectomy. Colorectal neoplasms.

INTRODUCTION

Liver resection is the treatment of choice for colorectal liver metastases, and several studies have shown long-term survival rates ranging from 40% to 57%. Many predictive factors for survival after liver resection have been studied, and hilar lymph node involvement, which is present in 2% to 10% of the cases, is associated with a poor prognosis. Although the results have been variable, some authors have shown long-term survival in liver-metastasis patients with hilar-lymph-node involvement who undergo liver resection and hilar lymphadenectomy. Due to the low rates of morbidity and mortality for liver-resection surgery, several specialized centers perform liver resections combined with lymphadenectomies in selected cases. The therapeutic value of systemic lymphadenectomy is not yet entirely understood, and only controlled studies comparing groups with and without lymphadenectomy can fully resolve the issue. However, hilar lymphadenectomy is a useful tool for improving extra hepatic-tumor staging independently of its impact on survival. The authors performed a review of systematic lymphadenectomy in patients who have undergone liver resection for colorectal cancer metastases.

Hepatectomy is currently the treatment of choice for hepatic metastases of colorectal cancer, and several studies have shown good results, with 5-year survival rates ranging from 40% to 57%[1, 2, 3, 5, 12].

Several clinical and pathological predictive factors for survival after hepatic resection have been studied. These factors include the locoregional staging of the primary tumor, the presence or absence of extra-hepatic disease, the interval between the diagnoses of the primary and the metastatic lesions, the pre-operative level of carcinoembryonic antigen and the lymph-node involvement of the hepatic hilum. Despite some discrepancies in results, most studies have shown that lymph-node involvement at the primary site, synchronicity of the lesions, four or more hepatic lesions, and hilar lymph node metastases constitute the major negative prognostic factors, with significant impacts on long-term survival[3, 28, 31, 30].

It is believed that lymph-node involvement in patients with colorectal liver metastases may actually constitute a tertiary metastasis or "metastasis of a metastasis", a concept proposed by August et al.[6] in 1985 and subsequently reinforced by other studies[10, 15]. The prevalence of macroscopic lymph node involvement in the hepatic hilum of patients with colorectal liver metastases varies between 2% and 10% in major series[6, 7, 12, 29], and they generally indicate a poor long-term prognosis. Based on these results, most authors have considered macroscopic lymph node involvement to be a contraindication to liver resection[13, 22, 32]. It

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should be remembered, however, that assessments based only on palpation and macroscopic inspection (the procedures used by most surgeons), and those based on an examination of frozen lymph-node sections suspected of metastatic involvement, are not accurate. Studies that have employed systematic dissection of suspicious and non-suspicious hilar lymph nodes to diagnose microscopic involvement have found an incidence of 15%[11, 20]. Studies that have examined the impact of microscopic lymph-node involvement on survival have found it to have a negative effect. Thus, the relevant question is whether hepatic resection is indicated in patients with affected hilar lymph nodes?

Despite a certain amount of controversy, some authors have reported significant survival rates in liver-metastasis patients with associated hilar-lymph-node disease who undergo combined liver resection and lymphadenectomy[7, 9, 16, 17, 25]. Among those results, Kokudo et al.[19] have shown that the survival rate of patients with lymph node disease who undergo curative resection and lymphadenectomy is significantly higher than that of residual-liver-disease patients without lymph-node metastases who undergo liver resection (17 months versus 8 months, $P<0.05$). These authors therefore suggest a possible benefit from resection and hilar lymphadenectomy in patients with lymph node involvement[7]. Two other studies have found 3-year survival rates between 38% and 45% in patients with compromised liver pedicle lymph nodes who undergo liver resection combined with lymphadenectomy. However, the authors call attention to the location of the compromised lymph nodes: when they are located near the hilum, the resection may offer long-term survival benefits, but when they are near the common hepatic artery or celiac trunk, the long-term survival is significantly worse[16, 17]. These authors emphasize that proximal lymph node involvement is not a contraindication to hepatectomy, which they defend under those circumstances. Recently, Adam et al.[4] described an 18% global 5-year survival rate in a selected group of patients with hepatic metastases and compromised hepatic hilar lymph nodes who underwent hepatic resection and lymphadenectomy. Due to the low rates of morbidity and mortality for liver-resection surgery, several specialized centers (including our facility) perform liver resections combined with lymphadenectomies in selected cases.

It should be noted that the therapeutic value of systemic lymphadenectomy is not yet entirely understood, and that only controlled studies comparing groups with and without lymphadenectomy can fully resolve the issue. In any case, hilar lymph node dissection has been shown to be a useful tool for improving the accuracy of extra hepatic disease staging, regardless of its impact on survival.

Recently, a microscopic study at our facility on lymph-node micrometastases, in patients without macroscopic lymph-node disease who undergo hepatic resection and lymphadenectomy, showed involvement of the hilar lymph nodes (including micrometastases) in 18% of the patients, which confirms the hypothesis that an examination restricted to the radiological and macroscopic aspects is inadequate as a complete evaluation and that lymph node dissection can improve the staging accuracy[33]. Moreover, lymph-node evaluation through multiple serial sections followed by immunohistochemistry staining using human pancytokeratin AE1/AE3 antibody detected a further 10.8% of the patients with micrometastases, all of whom were negative by conventional methods. Thus, the immunohistochemistry method was shown to increase the detection of affected lymph-nodes[33]. In a recent study, Bennet et al.[8] similarly used serial thin sections followed by immunohistochemistry in patients with colorectal hepatic metastases and diagnosed micrometastases in 24% of the samples. Micrometastases research has been routinely used in breast cancer and melanoma cases[14, 17, 18, 23, 24], and several studies on other malignancies have confirmed that it expands the diagnostic sensibility[21, 26, 27].

From a practical perspective, the clinical importance of lymph node micrometastases for long-term survival is not known, especially in patients undergoing systemic treatment (chemotherapy). There is a dearth of studies evaluating whether detecting micrometastases only allows for better staging, is indicative of a poor prognosis, or has limited prognostic value. Despite some authors having shown a correlation between the major prognostic factors and the presence of lymph node metastases[11, 17], most studies have not found such associations and have reaffirmed the impossibility of determining risk subgroups for hilar lymph node involvement[8, 19, 20, 33].

A controversial issue is the role of lymph node dissection in major-chain sampling without a complete dissection of the hepatic hilum and the celiac trunk. In 1999, Kokudo et al.[19] used this method to show a tendency towards 12B chain involvement in patients with metastases on the right side and towards 8A chain involvement in lesions located on the left side. Based on these findings, the authors concluded that this sampling method is effective for determining the lymph node status of a patient. However, other authors have not found a relationship between the chains involved and the topography of the hepatic lesions[7, 11, 17, 20]. In 1996, Elias et al.[11] diagnosed microscopic lymph-node involvement in several of the lymphatic chains studied without a continuous progression from one chain to another (lymph-node-jumping metastasis). Therefore, any specific lymph-node group will reflect the true state of ganglion involvement in patients with metastatic hepatic lesions.

Finally, it is important to highlight the possible role of systemic treatment in patients with macroscopic or microscopic lymph-node disease who undergo resection and lymphadenectomy. It is presumed that modern chemotherapy procedures, either preoperatively or as an adjuvant, can positively influence the clinical course of these patients, possibly creating a new paradigm for the treatment of colorectal liver metastases and extending the limits of liver resection, even in patients with lymph node involvement. However, controlled studies that compare groups with and without lymphadenectomies are required to obtain more consistent results and determine the real survival value of the procedure in patients with resectable colorectal liver metastases.

Viana EF, Herman P, Coelho FF, Taka TA, D'Albuquerque LAC, Cecconello I. Papel da linfadenectomia hilar em pacientes submetidos a hepatectomia por metástases colorretais. Arq Gastroenterol. 2011;48(3):217-9.

RESUMO – ***Contexto*** - A hepatectomia é o tratamento de eleição para metástases hepáticas de câncer colorretal e diversos estudos têm demonstrado bons resultados, com índices de sobrevida em 5 anos entre 40% e 57%. Vários fatores clínico-patológicos preditivos de sobrevida após a ressecção hepática têm sido estudados e o envolvimento linfonodal do hilo hepático, que varia entre 2% e 10%, confere a este grupo prognóstico reservado a longo prazo. ***Resultados*** - Embora com resultados variáveis, alguns autores têm relatado sobrevida não desprezível em pacientes com metástases hepáticas associada à doença linfonodal hilar submetidos a hepatectomia conjuntamente à linfadenectomia. Muitos centros especializados, embasados nos baixos índices de morbimortalidade da hepatectomia, realizam a ressecção hepática associada à linfadenectomia em casos selecionados. Cumpre ressaltar que o valor terapêutico da linfadenectomia sistemática ainda não é inteiramente conhecido e somente estudos controlados, comparando grupos com e sem linfadenectomia, poderão dirimir estas questões. ***Conclusão*** - De qualquer forma, a dissecção linfonodal hilar demonstrou ser uma ferramenta que torna mais preciso o estadiamento da doença extra-hepática, independente do impacto deste procedimento na sobrevida.

DESCRITORES – Metástase neoplásica. Linfadenectomia. Hepatectomia. Câncer colorretal.

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