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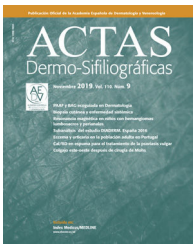

LETTER TO THE EDITOR

Sentinel Lymph Node Biopsy in Melanoma Does Have Therapeutic Utility☆

La biopsia selectiva del ganglio centinela en melanoma sí tiene utilidad terapéutica

To the Editor:

I read with interest the report by Espinosa-Pereiro et al.[1] on their study of the complications and sequelae after sentinel lymph node biopsy (SLNB) in routine clinical practice. The authors report high percentages of both complications and sequelae. This morbidity must be a consideration when evaluating with patients whether they should undergo the procedure and discussing the risk-benefit ratio in each case. The authors also highlight the fact that, following the publication of the results of the Multicenter Selective Lymphadenectomy Trial (MSLT) 2 and the DeCOG-SLT clinical trial, lymphadenectomy should no longer be considered the standard option in patients with a positive SLNB. This change in practice could reduce the complications and sequelae associated with the procedure in these patients. I recently discussed this issue in the present journal.[2] In the study by Espinosa-Pereiro et al.,[1] SLNB even when not followed by completion lymph node dissection (CLND) was associated with complications in 30.9% of cases and sequelae in 7.5%. I agree with those authors that this information should be taken into account by doctors and patients who are considering a procedure whose benefit, in most cases, lies only in the diagnostic and prognostic information it provides.

However, I disagree with them on one point that has considerable weight in the patient's decision. In the first sentence of their abstract, the authors state that ''SLNB is a staging, not a therapeutic, procedure''. In my opinion, this statement is inaccurate, does not take into account the available evidence, and is based on an incomplete understanding of the natural history of melanoma and the patterns of spread observed in these patients.

An excellent way of analyzing this question is to study the survival curves from the time, several decades ago, when we had no effective treatments for disseminated melanoma and no adjuvant treatments capable of significantly modifying the natural course of the disease. The key is to observe the survival of stage III patients at that time. Long-term survival was good in about one-third of stage III patients overall.[4] What does that mean? The answer is simple: in about one third of patients with lymphatic spread, the clinically relevant disseminated disease is exclusively lymphatic and when the affected regional nodes are dissected most of those patients are cured.

As I have discussed extensively in earlier articles,[2,3,5] clinical trials comparing early prophylactic lymph node dissection and CLND following a positive SLNB have never shown any therapeutic benefit on final survival compared to delayed therapeutic lymphadenectomy. But this does not mean that these forms of early lymphadenectomy are of no therapeutic value. What these results indicate is that, in terms of survival, they have no greater therapeutic utility than delayed therapeutic lymphadenectomy.[3] Obviously, any form of lymphadenectomy, whether prophylactic or therapeutic, will cure patients with melanoma in whom the spread is exclusively lymphatic, provided that the surgery targets the affected lymphatic basin and the metastasis is entirely confined to the area of intervention and has only affected the lymph nodes that are excised.

It is especially important to remember one fact about the therapeutic utility of SLNB: in around 80% of patients who have a positive SLNB no melanoma will be found in the remaining regional lymph nodes.[6] Consequently, this early intervention, which is simpler than delayed lymphadenectomy and associated with fewer complications and sequelae, resolves the problem of locoregional lymphatic spread in about 80% of patients in whom the sentinel node is positive, even without CLND.

Patients should be informed as clearly as possible of these facts. They should be made aware that in about one-third of patients with lymphatic spread, the clinically relevant disease will be exclusively lymphatic. And that for 80% of patients with exclusively lymphatic spread, SLNB will not only be diagnostic, it will also be curative since the surgery will remove the only important focus of metastatic melanoma from their body.

The model of stepwise spread in melanoma has been superseded: it was clearly incorrect and we now know that early intervention on the regional lymph nodes does not prevent the systemic spread of melanoma.[5,7–9] However, in around one-third of stage III patients systemic spread does not occur. And in 80% of these patients with exclusively lymphatic spread, SLNB can be curative (although we are, as yet, unable to identify these patients a priori). Furthermore, SLNB can facilitate the selection of patients for adjuvant

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treatment[10] since a positive biopsy is associated with an increased risk of systemic dissemination. Patients should be informed of all of these facts before deciding whether or not to undergo SLNB when this option may be indicated.

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Sentinel Lymph Node Biopsy Has No Therapeutic Value in Melanoma and Is Not Useful for Selecting Patients Who Could Benefit From Adjuvant Immunotherapy☆

Biopsia selectiva del ganglio centinela en melanoma: ni utilidad terapéutica, ni es buena para seleccionar los pacientes que podrían beneficiarse de la inmunoterapia adyuvante

To the Editor:

We thank Dr. Pizarro for the opportunity to discuss the usefulness of sentinel lymph node biopsy (SLNB) in the treatment of cutaneous melanoma. In his letter he makes several points. The first is that lymphadenectomy can be curative if the affected nodes are dissected.[1] We agree with this view: the survival curves to which he refers are not a description of the natural history of the disease (without intervention) but rather refer to patients who were followed up and in whom affected lymph nodes were excised when regional disease was detected. In this scenario, the alternative to SLNB is not inaction but rather observation and excision of affected nodes when metastasis is detected clinically or by ultrasound.

We also agree that SLNB has no effect on patient survival. In a huge study undertaken to determine whether SLNB increased survival—the Multicenter Selective Lymphadenectomy Trial (MSTL-1)[2]—1661 patients were randomized, starting in 1994, and were followed up for 10 years. This was such a remarkable effort that it is extremely unlikely to be repeated. The results of MSTL-1 provide a clear and definitive answer to the question posed above. The answer is that melanoma specific survival does not increase in patients who have undergone SLNB. And this is clear despite the optimistic biases that affected the reporting of MSTL-1, such as the authors' decision to ignore the study's primary outcome (the description of overall survival) to the extent that an unsuccessful request has been made for the raw data be made public so that it can be reanalyzed.[3] If undertaking SLNB has no beneficial effect on survival, why choose to undergo a surgical intervention that is expensive, invasive, and associated with the risk of morbidity?

Dr. Pizarro's argument is that, hypothetically, SLNB is a simpler procedure than delayed lymphadenectomy and

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