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Better Prognostic Models May Result in Improved Patient Selection for Adjuvant Therapies After Complete Resection of Solitary Fibrous Tumors of the Pleura

To the Editor:

We read with great interest the article by Bylicki et al.[1] on the multimodal management of solitary fibrous tumors of the pleura (SFTP). The authors present a multi-institutional series of 68 patients with SFTP, spanning a wide spectrum of presentation from localized to metastatic disease. They describe in detail applied perioperative therapies and follow-up data to illustrate treatment efficacy, which unfortunately was limited. The authors also highlight the importance of the classification proposed by de Perrot et al.[2] in the decision making for the administration of adjuvant therapies.

Excluding patients with metastatic disease (n = 9), there were 59 patients who underwent resection of SFTP as the primary treatment. Of these, five (8.5%) received perioperative treatments, mostly chemotherapy. Recurrence was observed in 18 (30.5%) patients with localized SFTP. Regardless of their stage classification, recurrence rates were extraordinarily high and not congruent with previous published series (recurrence: 4–15%)[2–5]; this observation seemed driven by the recurrence of 52% in de Perrot stage II tumors, which may invoke the completeness of resection. Unfortunately, it is not possible to discern from the study how many patients with localized SFTP underwent incomplete resection, and the impact this may have contributed to recurrence.

On the other hand, the authors stress the importance of the classification proposed by de Perrot et al.,[2] not only as a prognostic factor but also as a guideline for adjuvant interventions. It should be noted that this classification was based on a nonsystematic literature review, and despite its prognostic value, corroborated by the authors[1] and others, its validity to guide management after SFTP resection has yet to be proven. Moreover, management recommendations derived from this classification[2] were intended after complete resection, as patients with incomplete resections are at a higher risk for recurrence. Therefore, it is not surprising that adjuvant chemotherapy was given to six of seven patients with tumor invasion at the resection margins, regardless of their de Perrot classification.

Recently, a scoring system was proposed for the prediction of SFTP recurrence after complete resection[3] and was later validated in an independent European population.[4] This score combines six macroscopic and histopathologic tumor characteristics to classify patients according to their risk of recurrence with excellent predictive capacity, outperforming both the use of England's criteria and de Perrot's classification. A recent independent, multi-institutional series of patients with SFTP[5] found this scoring system to provide better discrimination compared with previously published classifications. In addition, this score has been associated with the extent of surgery, use of adjuvant therapies, and overall survival.[4] This scoring system was first published in 2013[3] and should be carefully considered by the authors to assess risk of recurrence in the analysis of their patient population. Better prognostic models, such as the one mentioned here,[3,4] may result in better stratification of patients according to their risk of recurrence. This would result in improved selection of those patients at the highest risk for SFTP recurrence for adjuvant interventions, clinical trials, or stricter postoperative surveillance protocols.

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The response below published previously in the June 2015 issue. It is republished below to appear with the Letter to the Editor by Drs. Tapias and Lanuti.

Reply to "Better Prognostic Models May Result in Improved Patient Selection for Adjuvant Therapies After Complete Resection of Solitary Fibrous Tumors of the Pleura"

In Response:

We would like to thank Dr. Tapias and Dr. Lanuti for their

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comments on our recent article reporting on a multicenter cohort of 68 patients with solitary fibrous tumors of the pleura (SFTP), who were analyzed for the complete course of the disease in a routine practice setting.[1] We acknowledge that our recurrence rate of 30% in nonmetastatic disease was higher than that previously reported in surgical series, including that by Tapias et al.[2] (14%). We hypothesize this may be related to (1) a more limited enrollment period (12 years from 2000 to 2012, versus 33 years from 1977 to 2010 in the Tapias series) together with (2) a prolonged median follow-up of 13 years and (3) the recruitment of cases from medical oncology services, at an advanced stage of the disease then requiring chemotherapy treatment.[1] We agree that incomplete resection may have contributed to this higher recurrence rate, as five patients—four stage II tumors, one stage III tumor—had R1 resection, and two patients—both stage III—had R2 resection. We believe this reflects routine practice, as other surgical series similarly reported incomplete resection to occur in 7% to 11% of malignant SFTP.[3]

On the basis of their series of 59 patients, Tapias et al. propose a scoring system to predict SFTP recurrences; four of the six variables of this scoring are actually common with that of the England/de Perrot staging, including structure, mitotic activity, cellularity, and presence of necrosis.[2] Of note, Tapias et al. did not applied the de Perrot staging to their cases, whereas they stated that scoring was a superior predictor of recurrence.

Comparing our cohort with this series, scores had the following distribution: 0 in 15% versus 42% patients, 1 in 13% versus 19%, 2 in 28% versus 19%, 3 in 19% versus 12%, 4 in 7% versus 5%, 5 in 9% versus 3%, and 6 points in 9% versus 0%. Scoring, although correlating with the de Perrot stage ($p < 0.001$), was also a significant predictor of recurrence-free survival ($p = 0.007$): 3-year, 5-year, 10-year, and 15-year recurrence-free survival rates were 40%, 31%, 25%, and 25%, respectively, for a score ≥3, and 88%, 70%, 58%, and 58%, respectively, for a score <3. These figures are far lower than that reported in the original series by Tapias et al.—80%, 69%, 23%, and 23% for a score ≥3 and 100% for a score of <3—and in a more recent validation cohort.[5] This reflects the higher aggressiveness of our cases that would be even more appreciated using the proposed 6-class score, which may be even more relevant for advanced malignant cases. Whether these analyses are relevant to drive perioperative management still remains to be determined, especially because the efficacy of adjuvant treatment is limited, as highlighted in our cohort.

Ultimately, such major differences between reported series of TFSPs emphasize the need for multicenter collaboration to develop prospective observational cohorts of consecutive patients, what remains challenging given the wide range of aggressiveness of the disease, the long-term survival of patients, and the multidisciplinary management from initial presentation to recurrent disease.

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No Increased Risk for Mesothelioma in Relation to Natural-Occurring Asbestos in Southern Nevada

To the Editor:

As cancer epidemiologists, we read the article by Baumann et al.[1] with great interest. We praise Baumann for producing a body of literature on mesothelioma and exposure to natural-occurring asbestos (NOA).[2–4] The recent discovery of NOA in Southern Nevada has raised our interest in the surveillance of mesothelioma in the region.

Unfortunately, in our opinion, the methodology used was inappropriate for the stated aim of the study: "to test that malignant mesothelioma is increased in Southern Nevada in a pattern consistent with environmental exposure." The proper indicator of risk in a population or a subpopulation is the incidence rate (gender specific, age adjusted, and/or age specific). Proportions or sex ratios restricted to mesothelioma deaths are not appropriate measures of risk because they do not account for the underlying population pool (and the concept of risk in epidemiology) from which the cases arise. For instance, a male to female sex ratio can be elevated just by virtue of a

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