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11<sup>th</sup> International Meeting on General Thoracic Surgery



Hospital  
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10<sup>th</sup> International Workshop on Surgical Exploration of the  
Mediastinum and Systematic Nodal Dissection



5<sup>th</sup> Meeting of the Thoracic Oncology, Thoracic  
Surgery, Techniques & Transplant, Respiratory Nursing  
and Respiratory Physiotherapy Areas of the Spanish  
Society of Pneumology and Thoracic Surgery (SEPAR)



3<sup>rd</sup> Joint Meeting of the Spanish Society of  
Thoracic Surgery (SECT)



30<sup>th</sup> Congress of the "Asociación Iberoamericana  
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10<sup>th</sup> International Workshop on Surgical Exploration of the  
Mediastinum and Systematic Nodal Dissection



## WHY THE MARS2 TRIAL DOES NOT MEAN THAT ALL MESOTHELIOMA IS UNRESECTABLE- THERE IS A FUTURE FOR MESOTHELIOMA SURGERY

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The published report of the MARS2 trial [1] suggested that the addition of extended pleurectomy/decortication to chemotherapy for pleural mesothelioma was harmful. Thus, the report goes on, all disease should be considered as unresectable and no further mesothelioma surgery for survival benefit should be considered.

This statement has changed clinical practice in UK, however, the design of the MARS2 trial has several limitations which should prevent its conclusions being over interpreted. These limitations include:

### Too Many

In the planning of MARS2 we were conscious of the problems in recruitment encountered in the initial MARS trial [2] and therefore were more liberal in the inclusion criteria. Whilst we recruited to MARS2 ahead of schedule there were consequences. Almost 1 in 7 patients were included with non-epithelioid mesothelioma, including 5% with pure sarcomatoid disease.

With a mean age of 69 years, many of the subjects were elderly and with a mean FEV1 of 75% many had significant COPD.

### Too Much

The surgical objective was simply to obtain macroscopic clearance of the tumour which was obtained in an impressive 84% of cases. However, very few patients had intentional preservation of the diaphragm. *Extended* pleurectomy decortication was performed in 83% even in those with no pathological involvement of the diaphragm.

The extent of surgery may have contributed to the excess early postoperative mortality which was related to pneumonia in most cases. It should also be noted that the excess in mortality in the surgical arm of the trial (12% v 6%) was not disease related. Indeed, there was no difference in the disease progression in the two groups.

### Too Late

Selection in the trial was based on the 7<sup>th</sup> TNM Edition of staging and in this context 56% had locally advanced disease. PET-CT was not mandated nor was histological confirmation of

mediastinal nodal status. Node positive disease was not an exclusion criterion and furthermore 4% of surgical patients had cM1 disease.

### 9<sup>th</sup> TNM staging

The latest 9<sup>th</sup> TNM staging for mesothelioma has modified the T component based on measurements of pleural thickness [3]. The cumulative thickness at 3 levels (Psum) and thickness of the interlobar fissure (Fmax) have been used have been shown to be of prognostic significance. Using this latest TNM staging, the median survival for stage I (T1N0) is 50 months and for stage II (T1N1 or T2N0) is 29 months with 40% alive at 3 years. Based on these results there does appear to be a reasonable case for offering surgical resection to these patients.

### Further subgroup analysis

Within a partial analysis of the MARS2 surgical cohort, we found that in 79 of the 158 patients who underwent pleurectomy decortication only 24 (30.3%) fulfilled these criteria: 8 were cT1N0; 9 cT1N1 and 7 cT2N0, all were epithelioid PM. The median survival of this group was 35 (1-72) months with 33% alive at 4 years. On postoperative staging only 10 (13%) remained in stage I/II.

In our post-MARS2 cohort we have found a survival benefit for diaphragm preservation in similar stage disease [5] and a detrimental effect from neoadjuvant platinum/pemetrexed chemotherapy in stage I and II disease [6].

### Conclusion

As contemporary selection criteria were not applied in MARS2 its conclusions cannot be universally applied to all those with PM. Together with the favourable postoperative survival in this selected group we suggest that there is still scope for a further trial of surgery in early-stage epithelioid mesothelioma.

### References

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