Ovarian cancer screening: searching for light at the end of the tunnel

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... Have you heard it? No, now you can’t hear it. Do you see it? All this fits in this instrument, theoretical and physically, only that cannot be obtained musically in practice. And same thing happens in the wind instruments. As well as in humans, figuratively, it means. I know many people who have a whole universe, infinite. However, can not boot them, much to attempt to.

Patrick Suskind, The bass.

In a previous article published in January 2016 in this portal, and entitled Screening research in ovarian cancer: analysis of the results of the study UKCTOCS\(^1\), with regard to the expected conclusion of the biggest series in ovarian cancer research carried out so far, most outstanding data from this study were analyzed\(^2\). The UKCTOCS reported a sensitivity for the diagnosis of ovarian cancer of 84% through the use of the determination of the levels of CA 125 and transvaginal ultrasound (TUS) as secondary test, called multi-modal screening group (MM), using the ROCA (Risk of Ovarian Cancer Algorithm) algorithm. Also in this same group the detection of primary peritoneal disease or ovarian cancer, with low volume, was larger and statistically significant to the diagnosed in the group with TUS only and non-screening group. On the other hand the reduction of mortality in the first seven years of the screening was 8% compared to 23% during the screening between 7 and 14 years, which could be related to the detection of new cases and not the prevalent within the sieved sample. With the exclusion of the prevalent cases of ovarian cancer, the mortality reduction was 20%, with 8% in the first seven years and 28% between 7 and 14 years of the screening, which was statistically significant reduction (p = 0.021).

As for the complication rate stood at 8.6 per 100,000 women in the MM Group compared to 18.6 per 100,000 women in the US Group. Were performed 14 unnecessary surgeries each 10,000 evaluations in the MM group compared to 50 for each 10,000 in the TUS group assessments, related with a benign adnexal disease or without any lesion. With these data, one of the main conclusions is that the use of the multimodal search (CA125/US) is much more effective and efficient than the use of the TUS only.
A letter to the editor, published in the first issue of May 2016 of the *International Journal of Gynecological Cancer* called *Ovarian Cancer Screening There May Be Light at the End of the Tunnel?* and written by Ranjit Manchanda and David Cibula, from Saint Bartolomew's Hospital in London and the Charles University in Prague, respectively. This letter, re-emphasizes the need to give it a new look, much deeper to the UKCTOCS results. Although in the analysis a non-statistically significant 15% reduction in mortality was achieved, they insist in the likely late effect in reduction of mortality after seven years of screening. The screening achieved an increase in the diagnosis of ovarian cancer stage IIIA or less from 26% to 40%, which was related to a greater probability of complete cytoreduction (R0) in the screening group. This finding, reported between the lines in the original manuscript, comes to bind properly to the robust actual trend of increasingly complex surgeries in order to achieve a debulking R0.

In one of the most important paragraphs of the letter the authors comment: *If screening is associated with an increase in lower volume disease, this may well lead to the need for proportionally fewer ultraradical surgical procedures with lower morbidity and potentially beneficial cost implications. At the same time, it remains unknown if screening also resulted in less bulky or lower-volume stage 3B/3C disease, which may be more amenable to achieving R0 resection and better outcomes. This is an important issue, and it would be helpful if this were further evaluated and reported by the research team.*

About the design of the UKCTOCS, commentators say that it must step not only to statistical prespecified analysis but design a statistical structure that allows the reliably estimation of the effect of reduction in mortality in the long run. Likewise considered that the use of the test of log-rank, in order to compare the reduction of mortality between the MM group and the control group, played down to statistical study and no was able to reliably determine the difference depending on the time, from random allocation to each group. Therefore recommended, in order to adjust or correct this deficiency, the use of more sensitive tests for the evaluation of alternative non-proportional odds and small differences between groups. They think that the original design could no longer detect one less than 30% difference between the arms, and the 14% rise in cases stages IIIA or less has been able to have an impact on reducing mortality of 30%.

At this moment the available results do not allow to justify the use of ovarian cancer screening within a national plan because of the lack of convincing evidence of a reduction in mortality, the non-negligible rate of complications and false positives, that still are the limiting major.

An efficient program of ovarian cancer screening should detect the disease in early stages or, in the case of an advanced tumor, a low volume neoplasia and this translates into better rates of complete cytoreduction. As described in the article, a successful strategy must be able to diagnose a tumor between 4 and 13 mm. This will be possible through the use of algorithms with additional biomarkers to the CA125, new technology in imaging and/or detection of circulating tumor DNA, a truly ambitious goal.

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References:
