

## Magnetic Resonance Imaging in Early Cervical Cancer: new perspectives

Jorge Sánchez Lander\*



*Don't do what you sincerely don't want to do. Never confuse movement with action.*

*Ernst Hemingway*

Radical hysterectomy (RH) remains the treatment of choice for cervical cancer stage IB1, with excellent disease-free and overall survival rates. However a group of these patients, with nodes and negative margins, will present criteria consistent with an increased risk of recurrence such as the lymphovascular invasion, tumor size and deep stromal invasion. Taking into account the criteria of Sedlis et al, it is considered that even a tumor just 1 cm in diameter with invasion lymphovascular and affection of the deep third of the cervical stroma will benefit from adjuvant external beam radiation<sup>1</sup>. However, this scheme which includes the RH and adjuvant radiotherapy has a rate of complications and sequelae in the medium and long term which is not negligible. For this reason a question arises from a few years ago an attempt to decrypt: Is it possible to predict in the preoperative evaluation of clinical, histopathological and imaging which patients will have criteria to receive adjuvant radiotherapy? On this point Charles Levenback wrote in 2003: *At M. D. Anderson, a fundamental factor influencing the decision regarding surgery versus radiotherapy for early cervical cancer is the likelihood that surgery would result in a recommendation for postoperative pelvic irradiation due to high-risk factors such as positive nodes, positive margins, or parametrial involvement. Pretreatment counseling should include an estimation of the risk of postoperative radiotherapy following radical hysterectomy. When the risk goes over 40% to 50%, our recommendation usually shifts towards primary radiotherapy*<sup>2</sup>.

In July 2016 it is published in *Gynecology Oncology* the article: *Treatment outcomes in patients with FIGO stage IB–IIA cervical cancer and a focally disrupted cervical stromal ring on magnetic*

*resonance imaging: A propensity score matching study*<sup>3</sup>. This interesting paper aims to analyze treatment outcomes and RH-related morbidity followed by adjuvant radiotherapy compared with those receiving radiotherapy with primary concurrent chemotherapy (RtCt) in patients with cervical cancer IB-IIA stages and With signs of focal disruption of the cervical stroma ring, in the axial sections MRI (weighted T2 sequences). From the structural point of view, the normal cervix is shown in the MRI, in axial T2 sequences, such as a circular image with a hyperintense center (endocervical mucosa) and a hypointense ring consisting of the cervical stroma. Focal rupture of the stromal ring (FRSR) has been associated with stromal infiltration and a high risk of incipient infiltration of the parametrium, undetectable physical examination<sup>4</sup>.

By using a retrospective study, Kong TW et al the of the Gynecologic Cancer Center of the University of Ajou in Suwon, Korea South, collected data on 156 patients diagnosed with cancer of the cervix (squamous cell, adenocarcinoma and adenosquamous) stage IB-IIA with FRSR in T2 axial oblique sequences. The total loss of the hypointense stromal ring was considered as a criterion of parametrial infiltration (stage IIB) and were excluded from the analysis. The images were obtained using a 3T resonator and a standard exploration protocol that included axial slices of the cervix in oblique form (perpendicular to the endocervical canal), in order to evaluate the stromal ring. On the RtCt arm 102 patients and 54 patients in RH arm were included. The patients in the RH group with two or more intermediate risk criteria in the biopsy of the surgical specimen (lymphovascular invasion, tumor size equal to or greater than 4 cm and stromal invasion greater than 50%), adjuvant radiotherapy were indicated. On the other hand, patients with node-positive, positive margins or microscopic parametrial invasion received external beam radiation with brachytherapy (in those with positive vaginal margins) a scheme of chemotherapy with 5-flouracilo and cisplatin. The average radiation dose was 4.930 cGy for adjuvant external beam radiation and 8,150 cGy in primary RtCt.

The statistical management of the sample allowed balancing the covariates in the two groups, reducing the effect of selection bias. Trends estimated scores were used to match the RtCt group with the RH group. Based on this statistical instrumentation, 54 patients who underwent primary RtCt were compared with 54 patients who received RH plus adjuvant radiation therapy.

As for the results, the local recurrence rate was 5.6% and 11.1% for the group of RtCt and RH plus adjuvant radiation therapy, respectively ( $p = 0.489$ ). As for distant recurrence was 7.4% in both groups ( $p > 0.999$ ). The total rate of relapse was 13% for group with RtCt and 20.4% for RH with adjuvant radiotherapy group ( $p = 0.302$ ). As can be seen while relapse rates are proportionately higher in the RtCt group, the difference did not reach to be statistically significant.

The incidence of late adverse effects to genitourinary level (grade 3) 0% in the RtCt group compared to 14.8% in the RH group was more adjuvant radiotherapy, a difference that was statistically significant ( $p = 0.006$ ). However, there was no difference in severe hematological complications (18.5% in the RtCt group vs. 22.2% in the group with RH and adjuvant radiotherapy,  $p = 0.633$ ); gastrointestinal 1.9% in the RtCt vs. 5.6% in RH and adjuvant radiotherapy group ( $p = 0.618$ ) or late lower limb lymphedema (grade 3) (3.7% in the RtCt group versus 13.0% in the group

with RH,  $p = 0,161$ ) between the two groups. Among the eight patients with genitourinary adverse effects, five were subject to urological surgical interventions. The five-year disease free survival showed no difference statistically valid, being of 83.1% to 77,4% for RtCt and RH group plus adjuvant radiation therapy respectively ( $p = 0.228$ ).

In the well documented discussion, the authors propose to use the criterion of the FRSR in the axial T2 sequences in MRI as an alternative to the low completeness in bimanual parametrial palpation, taking into account that the negative predictive value, in several series cited by the authors, is 94 %-100 %. In particular, in patients diagnosed with stage IB1 cervical cancer with tumors less than or equal to 3-4 cm presenting FRSR in the MRI, this finding was adequately related to parametric microscopic infiltration with a positive predictive value Of 72.2%.

In a series cited by the authors<sup>5</sup>, clinical and cost outcomes, including quality of life and cost of treatment of each complication, were estimated in a cost-utility analysis, they were confirmed to be less cost-efficient when added adjuvant chemoradiation. Therefore, bimodal treatment can be more expensive due to complications related to treatment and the decrease in quality of life.

Although it is a study with certain limitations in terms of the evidence and methodology used to adequately match the groups analyzed, it reflects a deep-rooted trend in highly experienced centers such as the MD Anderson Cancer Center, which recommends determining in the pre-evaluation treatment, in patients with IB-IIA stages, those criteria with a good specific weight that show a high probability that after radical hysterectomy will be required adjuvant radiotherapy in order to omit the intervention and to be inclined by radiotherapy with chemotherapy concurrently primary. This trend also leans on developing tools enabling to accurately recognize patients with disease less than 3-4 cm in diameter without FRSR and extracervical extension which would be the best candidates to undergo a radical hysterectomy as unique therapy, without the risk of having to indicate adjuvant radiotherapy, with its undeniable impact on tolerance and late morbidity profile. The modern perception of precision in oncology means not only not to fall short, but also not unreasonably exceeds the treatment.

\*Cirujano oncólogo, especialista en ginecología oncológica y mastología. Servicio de Ginecología Oncológica del Instituto de Oncología Luis Razetti y Clínica Santa Sofía, Caracas, Venezuela.

## References

1. Sedlis A, Bundy BN, Rotman MZ, Lentz SS, Muderspach LI, Zaino RJ. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. *Gynecol Oncol* 1999;73(2):177-83.
2. Levenback Ch. Treatment of Early Cervical Cancer. En *Gynecology Oncology*, MD Anderson Cancer Care Series , P.J. Eifel, D.M. Gershenson, J.J. Kavanagh, and E.G. Silva, Springer, New York 2006.

## Intervalibre

3. Kong TW, Lee JD, Son JH, Paek J, Chun M, Chang SJ, Ryu HS. Treatment outcomes in patients with FIGO stage IB–IIA cervical cancer and a focally disrupted cervical stromal ring on magnetic resonance imaging: A propensity score matching study. *Gynecol Oncol* 2016; 143: 77–82.
4. Kaur H, Silverman PM, Iyer RB, Verschraegen CF, Eifel PJ, Charnsangavej C. Diagnosis, staging, and surveillance of cervical carcinoma. *Am J Roentgenol* 2003; 180: 1621–1631.
5. Katanyoo K, Praditsitthikorn N, Tangjitgamol S, Manusirivithaya S, Supawattanabodee B, Cost-utility analysis of treatments for stage IB cervical cancer. *J Gynecol Oncol* 2014; 25: 97–104.