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Editorial

New developments and controversies in cervical cancer

This special issue of *Reports of Practical Oncology and Radiotherapy* explores a wide range of issues surrounding the treatment of cervical cancer (CC), which is the 4th most common cancer in women worldwide and is particularly prevalent in underdeveloped and developing countries.[1] Since the early 20th century, radiotherapy has been used as a curative intent treatment in non-surgical cases and as an adjunct treatment in the postoperative setting. Early radiotherapy techniques consisted of orthovoltage X-rays and radium brachytherapy, which achieved 5-year survival rates of 30% in the 1930s, although treatment-related toxicity was substantial.[2] Improvements in surgical techniques, together with the emergence of cobalt-60 radiotherapy, further increased survival rates, although the late complication rate remained significant. Subsequent advances in radiotherapy included the development of linear accelerators, three-dimensional (3D) planning procedures, and afterloading source projectors for brachytherapy (initially for medium and low-dose rate sources and later for high-dose rate [HDR] sources). These improvements increased 5-year survival rates to 40–50%. At the end of the 1990s, new developments included intensity-modulated radiotherapy (IMRT) and 3D-planning for brachytherapy, with a greater use of iridium sources for HDR and pulsed-dose rate treatments.[3] The concomitant use of cisplatin-based chemotherapy with external beam radiotherapy (EBRT) further increased 5-year survival rates by as much as 10%. At present, chemotherapy plus radiotherapy is the treatment of choice for large tumors (>4 cm).[4] The clear association between human papillomavirus (HPV) and CC, which was identified as the leading cause of CC in recent decades, has led to the development of highly-effective vaccines. Although these vaccines are available in most developed countries, their routine administration implies a substantial cost, an issue that is explored in a cost analysis study presented in this issue.[5]

In recent years, there has been an exponential increase in the number of procedures available to manage CC. At the same time, new imaging techniques developed over the last 20 years have improved both the diagnosis and treatment of this disease. These imaging techniques have been particularly valuable to improve radiotherapy planning. Sentinel node evaluation is now routinely included in surgical practice to tailor pelvic lymphadenectomy in early stage disease to reduce patient morbidity, as discussed in detail by Glickman et al. in this special issue.[6] Indeed, magnetic resonance imaging (MRI) is now considered the gold standard for volume definition in planning both EBRT and brachytherapy; in this regard, this special issue includes two papers that describe the imaging techniques for treatment planning in patients with CC.[7,8] At present, MRI and PET-CT are considered the best imaging tools for patient follow-up. Moreover, pre- and post-treatment imaging data obtained via MRI and PET-CT can provide valuable information—together with molecular markers—to better establish prognosis and predict treatment outcomes.

Currently, IMRT is considered the optimal radiotherapy approach to minimize treatment-related complications in the postoperative setting. Although several clinical trials are currently underway, numerous studies have already demonstrated the benefits of IMRT for curative treatment.[9] Despite the many advantages of IMRT, this technique requires the daily use of image-guidance (mainly in advanced, non-surgical cases) to ensure accurate delivery of the radiotherapy.[10] It is highly likely that image-guided adaptive radiotherapy will become more widespread in the near future. Soft tissue matching remains under investigation.

The new European Society of Gynecological Oncology (ESGO)–European Society for radiotherapy and Oncology (ESTRO)–European Society of Pathology (ESP) guidelines for CC describe the use of paraaortic irradiation and the benefits of neoadjuvant/adjuvant chemotherapy, which are areas of controversy in the treatment of CC. In this special issue, three different articles address these treatment modalities.[4,11–13] The results of the ongoing EMBRACE II, NRG GY006 (Phase II), and INTERTECC trials are expected to resolve the current controversies related to numerous different aspects of treatment delivery, treatment related toxicity and multimodal treatment.

Brachytherapy combined with EBRT is the most relevant treatment in CC since it allows for the delivery of the highest dose to the tumor, thus providing greater local control and improving survival with fewer complications versus EBRT alone. After 2005, the Gynecological GEC-ESTRO working group published guidelines for MRI-based volume definition and for parametrial implantation. Several studies performed by this working group established MRI image-guided adaptive brachytherapy (IGABT) as the gold standard for the treatment of CC given that this technique yields better local control and survival than previously reported results using other techniques, with fewer treatment-related complications. Nonetheless, MRI-IGABT is much more time-consuming than other techniques and needs an experience and highly-trained team of radiation oncologists and physicists for proper implementation. One report in this issue describes the medical outcomes and other aspects of this procedure, while two other articles describe the radiobiological considerations related to the combined doses from both treatments and strategies for MRI-based endocavitary and interstitial reconstruction.[14–16]

One of the articles included in this issue describes newer treatment techniques such as stereotactic body radiotherapy (SBRT), which has several indications in CC (and is likely to have additional indications in the near future). At present, when brachytherapy is not feasible, SBRT appears to be a better option than IMRT alone; moreover, SBRT is an excellent option to treat nodal relapse.[17]

Combined treatment with immunotherapy and molecular therapies is currently being investigated to improve local control and survival in both curative and palliative patients. It appears likely that individualized treatment will be available in the near future. At present, neoadjuvant and adjuvant chemotherapy should be considered investigational in CC, which explains why chemotherapy is usually only considered to treat recurrent disease.[11,12,18] However, radiotherapy also plays a role in recurrent CC in which SBRT and hyperthermia and intraoperative radiotherapy have all been used, as discussed in two articles in this issue.[19,20]

We believe that readers will find that this special issue of RPOR provides a comprehensive exploration of the main aspects and controversies in the treatment of cervical cancer. These articles have been written by experienced clinicians and will undoubtedly provide readers with a greater understanding of the most relevant issues.

Conflict of interest

None declared.

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