ORIGINAL ARTICLE

Use of squamous cell carcinoma antigen in the management of cervical cancer

Uso do antígeno do carcinoma de células escamosas no manejo do câncer cervical

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ABSTRACT

Introduction: No tumor marker is recommended in the available guidelines for prognostic evaluation, treatment monitoring, and follow-up of patients with cervical cancer. However, the squamous cell carcinoma antigen (SCC-Ag) may play a role as a prognostic factor in the disease. **Objective:** To carry out a survey with Brazilian gynecologic oncology specialists on their knowledge and use of SCC-Ag in clinical practice. **Methods:** This was a transversal epidemiological study based on the application of a questionnaire developed on the Google Forms platform, comprised of three questions about the knowledge and use of SCC-Ag in the clinical routine of gynecologic oncology specialists. **Results:** The questionnaire was sent to 50 gynecologic oncology specialists, and the response rate was 80%. A total of 62.5% (n=25/40) of respondents reported knowing SCC-Ag. However, when asked about the use of SCC-Ag as a prognostic marker during the management of cervical cancer, 36 (90%) specialists stated that they had never requested it. Informed about the cost of the exam, 27 (67.5%) declared that they would request biomarker analysis in their clinical routine. **Conclusion:** SCC-Ag is the most widely studied tumor marker as a prognostic factor in cervical cancer, but it is underutilized by Brazilian gynecologic oncology specialists, despite their knowledge of this marker and willingness to request it.
Keywords: cervical cancer; antigens; prognostic factor.

RESUMO

Introdução: Nenhum marcador tumoral é recomendado nas diretrizes disponíveis para avaliação prognóstica, monitoramento do tratamento e acompanhamento de pacientes com câncer cervical. No entanto, o antígeno do carcinoma espinocelular (SCC-Ag) pode desempenhar um papel como fator prognóstico na doença. **Objetivo:** Realizar um levantamento com especialistas em oncologia ginecológica brasileiros sobre o conhecimento e a utilização do SCC-Ag na prática clínica. **Métodos:** Trata-se de um estudo epidemiológico transversal baseado na aplicação de um questionário desenvolvido na plataforma Google Forms, composto por três questões sobre o conhecimento e a utilização do SCC-Ag na rotina clínica dos especialistas em oncologia ginecológica. **Resultados:** O questionário foi enviado a 50 especialistas em oncologia ginecológica e a taxa de resposta foi de 80%. Um total de 62,5% (n=25/40) dos entrevistados relataram ter conhecimento sobre o SCC-Ag. Porém, quando questionados sobre a utilização do SCC-Ag como marcador diagnóstico ou prognóstico durante o manejo de pacientes com câncer cervical, 36 (90,0%) especialistas afirmaram que nunca haviam solicitado. Informados sobre o custo do exame, 27 (67,5%) declararam que solicitariam a análise do biomarcador em sua rotina clínica. **Conclusão:** O SCC-Ag é o marcador tumoral mais estudado como fator prognóstico no câncer cervical, mas é subutilizado pelos especialistas brasileiros em oncologia ginecológica, apesar de seu conhecimento e disposição em solicitá-lo.
Palavras-chave: câncer cervical; antígenos; fator prognóstico.

INTRODUCTION

Cervical cancer (CC) is the fourth most common type of tumor in the female population worldwide, with approximately 604,000 new cases annually, 85% of these occurring in developing countries. The disease can be classified into different histological subtypes, with squamous cell carcinoma accounting for 80% of cases[1].

Depending on the stage at the time of diagnosis, CC will recur in 25 to 61% of patients, with recurrences usually being diagnosed within two years of the end of treatment[2]. They most commonly recur in the central pelvis, lateral pelvic wall, and pelvic and para-aortic lymph nodes[2]. Tumor regression after radiochemotherapy may take three months; however, it is often difficult to identify with gynecological examination, imaging tests, or biopsy due to actinic and anatomical changes in the pelvis, which can cause false-positive results[3]. Therefore, other methods are needed to detect relapses and define a prognosis.

The squamous cell carcinoma antigen SCC-Ag has been considered the most important biomarker in CC since its description in 1977[4]. SCC-Ag is a subfraction of the TA-4 tumor antigen and belongs to the serine protease inhibitors (serpin) superfamily. Studies associated high pre-treatment SCC-Ag with more advanced disease, larger tumor size, lymph node involvement, angiolymphatic and deep stromal invasion, and consequently, a higher rate of recurrence and worse survival in CC patients[5-8].

Currently, no tumor marker is recommended in the available guidelines for prognostic evaluation, treatment monitoring, and follow-up of CC patients. However, studies have found that SCC-Ag may play a role in the early detection of tumor recurrence, response to therapy, and mortality[9-11]. Due to the importance of this marker, this study sought to survey Brazilian gynecologic oncology specialists on their knowledge and use of SCC-Ag in clinical practice.

OBJECTIVE

To carry out a survey with Brazilian gynecologic oncology specialists on their knowledge and use of SCC-Ag in clinical practice.

METHODS

A closed questionnaire was developed on the Google Forms platform and distributed between January 9 and June 16, 2023. The questionnaire consisted of three questions about the knowledge and use of SCC-Ag in the clinical routine of doctors who were part of the Brazilian Group of Gynecological Oncology. The questionnaire was sent via the WhatsApp application to gynecologic oncology specialists whose contact information was obtained from the Brazilian Group of Gynecological Oncology.

The following questions were asked:

1. Do you know about squamous cell carcinoma antigen (SCC-Ag)?
2. Have you ever used SCC-Ag as a diagnostic or prognostic marker during the management of patients with cervical cancer?
3. Considering the cost of the exam, around 350 Brazilian reais, would you use SCC-AG as a marker in your clinical routine?

RESULTS

The questionnaire was sent to 50 Brazilian gynecologic oncology specialists, and the response rate was 80%.

A total of 62.5% (n=25/40) of respondents reported having knowledge of SCC-Ag. However, when asked about the use of SCC-Ag as a diagnostic or prognostic marker during the management of CC patients, 36 (90%) specialists stated that they had never requested it. Informed about the cost of the exam, 27 (67.5%) declared that they would request biomarker analysis in their clinical routine.

DISCUSSION

Based on the questionnaire answered by members of the Brazilian Group of Gynecological Oncology, it was observed that most interviewees were aware of SCC-Ag; however, only 10% had already requested the exam in their clinical routine. After disclosing the cost of the exam and then asking about their desire to request the marker, most respondents stated that they would request it. There are no other surveys available evaluating the use of SCC-Ag in clinical practice.

SCC-Ag has been intensively studied as a tumor marker for squamous cell carcinoma. The available literature reveals that SCC-Ag has the potential as a reference indicator for evaluating CC biological behavior. A systematic review and meta-analysis of 61 studies showed a consistent association between SCC-Ag serum level and the results of relapses and survival of CC patients, reinforcing its use as a prognostic marker in clinical practice[9]. Another systematic review of 17 articles assessed the significance of SCC-Ag in the prognosis of CC and found that high marker values were associated with worse overall survival rate (hazard ratio [HR] 2.73; 95% confidence interval [CI] 1.48−5.05; p=0.001)[12].

A Chinese study investigated the clinical value of pretreatment serum of SCC-Ag in the administration of consolidation chemotherapy in CC patients undergoing postoperative extended-field radiotherapy and concurrent chemotherapy. The patients who received consolidation chemotherapy showed significantly better disease-free survival, and the pretreatment serum SCC-Ag>6.5 ng/mL was a predictive factor for the use of consolidation chemotherapy[13].

SCC-Ag levels can assist physicians in making decisions. Failure to normalize posttreatment SCC-Ag levels might predict tumor relapse. For these patients, adjuvant therapies should be considered.

SCC-Ag is recognized as a highly reliable serum CC tumor marker and can also be used as an independent predictor of overall survival, disease-specific survival, and distant metastasis during treatment. However, the absence of guidelines in the European Society of Gynaecological Oncology, European Society for Medical Oncology, American Society of Clinical Oncology, and The National Comprehensive Cancer Network stands out as a factor for its limited use. Additionally, SCC-Ag is not covered by the Brazilian Unified Health System and some health insurance plans.

The failure to incorporate this marker into guidelines highlighted the lack of robust evidence supporting its efficacy and usefulness in CC assessment and treatment. This suggests that there are still significant gaps in understanding the role of SCC-Ag, requiring further research to validate its clinical applicability.

Strength

It is the first time that a survey has been carried out to evaluate the use of SCC-Ag in clinical practice.

Limitations

Limitations of the present study include the small number of participants which compromises the validity of the results and the ability to generalize to a broader population of experts. Furthermore, the formulation of the questions in the questionnaire administered via Google Forms could have been more comprehensive and detailed in order to obtain more significant insights into the knowledge and use of SCC-Ag in clinical practice.

CONCLUSION

SCC-Ag is the most widely studied tumor marker as a prognostic factor in CC, primarily in Asian countries. It correlates with disease extent and response to treatment, and provides a valid tool for early detection of recurrence. SCC-Ag is underutilized by Brazilian gynecologic oncology specialists despite their knowledge of this marker and willingness to request it. More Western studies are needed to corroborate the Eastern findings and define the use of this marker in guidelines and clinical practice.

Approval by the Human Research Ethics Committee

The study was approved by the Research Ethics Committee of the Lutheran University of Brazil/RS under document number 5776591. Informed consent was sent to the respondents of the questionnaire.

Contribution of each author

LAGZ: Conceptualization, Data curation, Formal analysis, Investigation Methodology, Project administration, Writing – review & editing. DS: Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. RR: Visualization, Writing – original draft, Writing – review & editing.

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