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#### **ORIGINAL ARTICLE**

# Serrated polyps and their association with synchronous advanced colorectal neoplasia\*



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#### **KEYWORDS**

Colonic polyps; Colonic neoplasms; Serrated polyps; Advanced colorectal neoplasia; Colonic adenoma; Advanced adenoma; Cross-sectional studies

#### **Abstract**

Introduction: Large serrated polyps (SP), proximal SP, SP with dysplasia and the presence of multiple sessile serrated adenomas/polyps (SSA/P), which we refer to as SP with increased risk of metachronous lesions (SPIRML), have been associated with an increased risk of advanced colon lesions on follow-up. It is unclear, however, whether SPIRML are also associated with an increased risk of synchronous advanced colorectal neoplasia (ACN).

Aim: The aim of this study was to estimate the prevalence of SPIRML and to evaluate the association between SPIRML and synchronous ACN.

Methods: A cross-sectional population-based study in all patients (1538) with histological diagnosis of SP obtained from colonoscopies, sigmoidoscopies and colonic surgery performed in Navarra Health Service hospitals (Spain) in 2011. Demographic parameters and synchronous colonic lesions (adenomas, advanced adenomas [AA] and ACN) were analysed.

Results: One fourth of the sample (384 patients) presented SPIRML. These were older patients, with a slight predominance of women, and with no differences in body mass index (BMI) compared to patients without SPIRML. In the univariate analysis, patients with SPIRML showed an increased risk of adenoma, AA and ACN. In the multivariate analysis, the SPIRML group had a higher risk of synchronous AA and ACN (odds ratio [OR]: 2.38 [1.77–3.21] and OR: 2.29 [1.72–3.05], respectively); in the case of ACN, this risk was statistically significant in both locations (proximal or distal), with OR slightly higher for the proximal location. Different subtypes of SPIRML had a higher risk of AA and synchronous NA.

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*Conclusion*: SPIRML were common in patients with SP, and their presence was associated with an increased risk of synchronous ACN.

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#### PALABRAS CLAVE

Pólipos de colon; Neoplasia de colon; Pólipos serrados; Neoplasia avanzada de colon; Adenoma de colon; Adenoma avanzado de colon; Estudio transversal

#### Pólipos serrados y su asociación con neoplasia avanzada de colon

#### Resumen

Introducción: Los pólipos serrados (PS) grandes, PS proximales, PS con displasia y la presencia de múltiples adenomas sésiles serrados (P/ASS), que englobamos bajo el término PS con riesgo aumentado de lesiones metacrónicas (PSRALM), se asocian a un mayor riesgo de presentar dichas lesiones, pero desconocemos si también se asocian a un mayor riesgo de neoplasia avanzada de colon (NA) sincrónica.

Objetivo: Estimar la prevalencia de PSRALM y evaluar la asociación con NA sincrónica.

*Métodos*: Se trata de un estudio transversal de base poblacional que incluyó a todos los pacientes (1.538) con diagnostico histológico de PS de muestras procedentes de colonoscopias, rectosigmoidoscopias e intervenciones quirúrgicas de los hospitales públicos del Servicio Navarro de Salud durante el año 2011. Se analizaron parámetros demográficos y presencia de lesiones sincrónicas de colon (adenomas, adenomas avanzados [AA] y NA)

Resultados: La cuarta parte de los pacientes (384) presentaron PSRALM, con una edad media más avanzada, un ligero predominio en mujeres y sin diferencias en cuanto al IMC respecto a los pacientes sin PSRALM. En el análisis multivariante el grupo PSRALM presentó un mayor riesgo de AA y NA sincrónicos (OR: 2,38 [1,77-3,21] y OR: 2,29 [1,72-3,05] respectivamente) y en el caso de NA, este riesgo fue estadísticamente significativo en ambas localizaciones (proximal y distal), con OR superior para la proximal. Los distintos subtipos de PSRALM presentaron un mayor riesgo de AA y NA sincrónicos.

Conclusión: Los PSRALM fueron frecuentes entre los pacientes con PS y se asociaron a un mayor riesgo de presentar NA sincrónica.

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#### Introduction

Colorectal cancer (CRC) is one of the most common cancers in Western countries, and is the second most common cause of cancer death in the United States and Europe. Epidemiological, molecular and genetic studies undertaken in the last 2 decades have broadened our understanding of this disease. These studies have shown that CRC, hitherto considered a homogeneous entity, is in fact heterogeneous in both its oncogenesis and development, and treatment and prevention strategies have changed accordingly.<sup>1</sup>

CRC usually progresses from known precancerous lesions such as colon polyps. The term colon polyp includes colon adenomas, serrated polyps (SP) and a heterogeneous group of lesions that include different types of polyps – inflammatory, hamartomatous, juvenile, etc. SPs were initially differentiated, from a histological perspective, into hyperplastic polyps (HP) and serrated adenomas (described by Longrace and Fenoglio-Preiser in 1990). Later, in 2002, Torlakovic et al. sub-classified serrated adenomas into sessile serrated adenomas (TSA). Finally, the new World Health Organisation (WHO) classification includes these polyps within the denomination SP, and classifies them into 3 histological types: HPs, SSA/Ps (with and without dysplasia) and TSAs. 4

Colon adenomas were previously considered to be preneoplastic lesions that could progress to CRC through the adenoma-carcinoma sequence, whilst HPs were considered harmless lesions, with no risk of becoming malignant. However, in the last 2 decades, thanks to improved genetic and molecular understanding of the pathogenesis of CRC, the efforts made by pathologists to standardise diagnostic criteria, and the qualitative and technological improvements made in colonoscopy, the malignization of SPs has been reconsidered, and they are now believed to progress via the serrated pathway to CRC, with this route being responsible for 15-30% of CRCs.<sup>5,6</sup> However, not all SPs will progress to CRC. The natural history of SPs and the genetic-epigenetic changes that cause them to progress to CRC are still unclear, so at present, SPs that will follow a benign course cannot be differentiated from those that will evolve to CRC. Furthermore, the consideration of SPs as precancerous lesions has also led to a change in CRC prevention strategies. While there were no specific recommendations for postpolypectomy endoscopic surveillance of SPs prior to 2010, in the last 5 years, some authors and scientific societies have stressed the importance of considering SPs as preneoplastic lesions, and advise taking them into account in screening programmes.

In this respect, several authors and scientific societies<sup>7-10</sup> have recently highlighted certain characteristics of SPs that

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