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Original Article

A prospective, multicenter analysis of pseudocapsule characteristics: Do all stages of renal cell carcinoma have complete pseudocapsules?

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Abstract

Objectives: To assess the characteristics of pseudocapsule (PC) in localized renal cell carcinoma (RCC) by analyzing the rates of completeness of PC and pseudocapsular invasion and clinical and pathological risk factors of it.

Materials and methods: Between February 2013 and September 2015, data were gathered prospectively from 180 consecutive patients who underwent partial nephrectomy or radical nephrectomy at 3 institutions, and 161 were enrolled. Evaluated factors included age and sex; histologic factors such as tumor diameter, stage, tumor subtype, necrosis, and Fuhrman grade; and clinical factors such as RENAL score; and completeness of PC.

Results: Only 94 tumors (58.4%) were surrounded by a continuous PC completely, 62 (38.5%) were partially surrounded, and 5 (3.1%) had no PC. Overall, 56 PCs (34.8%) were free from invasion, 58 PCs (36.0%) had partial invasion of PC without parenchymal invasion, and 47 PCs (29.2%) had parenchymal invasion. Defining parenchymal invasion as true pseudocapsular invasion, histologic diameter, RCC subtype, and completeness of PC were significant predictors for parenchymal invasion on multivariate analysis ($P = 0.006$, 0.046, and 0.002, respectively).

Conclusions: Rate of complete PC in RCC is relatively low in this study. The risk factors for pseudocapsular invasion were a histologic diameter greater than 4 cm, non–clear cell histology, and an incomplete PC. Surgeons must prepare for the possibility of a positive surgical margin if a tumor has at least one of these risk factors.

Keywords: Kidney neoplasms; Partial nephrectomy; Pseudocapsule

1. Introduction

The purpose of partial nephrectomy (PN) is to perform complete tumor removal with negative surgical margins (SMs) while preserving the maximum amount of healthy, vascularized renal tissue. Historically, the standard technique of PN involved excising a 1-cm margin of renal parenchyma to achieve a reliable negative margin and

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minimize the risk of local recurrence. This arbitrary 1-cm SM was introduced in 1950 by Vermooten [1]. However, a recent series report indicated that tumor margin width during PN is not associated with the likelihood of local recurrence. If a negative margin is achieved, even a 1-mm margin width is adequate and oncologically equivalent to a 1-cm margin width [2–5].

Tumor enucleation (TE) consists of bluntly dissecting the pseudocapsule (PC) of the renal tumor along a natural plane from the surrounding tissue without removing a rim of renal parenchyma [6]. In contrast, conventional PN consists of sharply cutting a thin rim of renal parenchyma along with the tumor. Several studies have shown that TE not only is oncologically safe with maximal preservation of renal parenchyma but also appears to provide technical benefits, including reduced entry into the renal sinus, less need for tumor bed suturing, and shorter operative time in cases of T1a renal cell carcinoma (RCC) [6–9]. However, the oncologic safety of TE remains controversial, as the technique could potentially result in a higher rate of local recurrence by inducing a positive SM [10].

With the evidence of comparable oncologic outcomes of PN and the risk of de novo renal failure after radical nephrectomy (RN) for a small renal tumor, the attention is now focused on expanding and setting the indications of PN in larger tumors. Recent reports have shown that PN achieves local tumor control equivalent to RN for RCC with a diameter of 4 to 7 cm [11,12], and the recent European Association of Urology guidelines expanded its indication to include solitary RCC up to a diameter of 7 cm, whenever technically feasible [13]. Given that tumors with larger diameters are located deeper in the renal parenchyma, certain surgeons tend to use TE rather than PN, intentionally or unintentionally, owing to concerns related to functional outcome and the risk of damage to renal vessels and collecting systems during PN for larger RCC.

The aim of this study was to assess the characteristics of PC in T1a and larger RCC by analyzing the rates of completeness of PC and pseudocapsular invasion and clinical and pathological risk factors for pseudocapsular invasion in RCC.

2. Materials and methods

2.1. Study population

This research was designed as a prospective multicenter study. After obtaining approval from the institutional review board of each institution, data were gathered prospectively between February 2013 and September 2015 from 180 consecutive patents with RCC who underwent PN or RN at 3 institutions in Korea. Overall, 15 patients with a pathologically proven benign tumor, 3 patients with a positive SM after PN, and 1 patient who refused to participate in the study were excluded.

2.2. Pathologic assessment

Before this prospective study, all of the urologists and dedicated uropathologists at each institution participated in several consensus meetings to determine the study protocol and histologic assessment of PC status. In cases of smaller tumors ($\leq$4 cm), all specimens were step-sectioned at 5-mm intervals, entirely embedded in paraffin blocks, and stained with hematoxylin and eosin for microscopic examination. In cases of larger tumors, thorough gross examination of the PC including pseudocapsular invasion and completeness of PC was performed by the uropathologist with the operator after 5-mm interval step-sectioning. If there was definite parenchymal invasion, several sections from invasion foci with representative sections from the largest plane of the tumor were submitted. Otherwise, entire sections including the tumor-PC-parenchyma interface and representative sections from the largest plane of the tumor were submitted (Fig. 1). Additionally, several histologic factors were assessed: pathological stage according to the 2010 American Joint Committee on Cancer TNM staging system [14], histologic subtype according to the World Health Organization 2004 classification [15], tumor grade according to the Fuhrman criteria [16], and presence of tumor necrosis.

2.3. Definition of PC

In this study, a peritumoral PC was defined as a parallel band of fibrocollagenous connective tissue located at the interface of the tumor and adjacent normal renal parenchyma, which could be verified on Masson's trichrome staining. Peritumoral PCs were subdivided as "intrarenal" and "extrarenal". We focused on "intrarenal PCs" defined by Azhar et al. [17], and "PCs on the parenchymal kidney side" defined by Minervini et al. [18,19], and excluded "extrarenal PCs" and "PCs on the perirenal adipose tissue side" (Fig. 1C) from our analysis.

2.4. Definition of completeness of PC

A PC was regarded as "complete" if it was intact without disconnection along its whole length despite any narrowing of width. A PC was regarded as "partial (incomplete)" if certain areas showed a disconnection of well-defined PC without parenchymal invasion (Fig. 2). A completeness of PC classification of "none" was defined as a PC that was not visible at any point along the whole tumor length such that the neoplastic cells directly interfaced with the renal parenchyma without any fibrous band.