Growth patterns of colorectal cancer liver metastases and impact on prognosis: a systematic review

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Summary:
Colorectal cancer liver metastases (CRLM) grow in distinct histological patterns that have been associated with outcome after surgical resection. We conducted a systematic review to evaluate the frequency of different CRLM growth patterns (GPs) and their impact on prognosis.

Narrative analysis suggested prognostic potential of CRLM GPs (Figure 1). Further understanding of the distinct GPs may provide important insights into the biological mechanisms that underlie metastatic growth in the liver.

Introduction
Approximately half of all colorectal cancer (CRC) patients develop metastases during the course of their disease, at which point survival rates drop markedly. The liver is the main target organ for CRC metastases. Several studies have suggested that distinct metastatic GPs are associated with differences in tumour recurrence and overall survival. We conducted a systematic review including 2,058 patients (Figure 2) and assessed the impact of the GPs on outcome.

Figure 1: Impact of main GPs on prognosis. First column: The encapsulated pattern is characterized by a rim of fibrotic stroma (green) that separates tumour cells from the surrounding hepatocytes; second column: In the replacement pattern, tumour cells (grey) invade along the liver cell plates, replacing the hepatocytes (yellow); third column: In the pushing pattern, the liver plates adjacent to the metastases appear flattened (arrowheads); Blue: central veins. a) Dot plot of all studies reporting outcome for the respective pattern indicated above the plot; one dot corresponds to one study; b) as in (a), but only considering studies published prior to FDA approval of Bevacizumab.

Figure 2: Study flow diagram according to the PRISMA criteria.

Nomenclature varied markedly across studies from the 1990s until today (Figure 3), precluding formal meta-analysis.

Figure 3: Word cluster diagram of GP terminology. Original terms for the histological GPs in the literature (n=22 studies) are shown with a font size proportional to their absolute frequency. The filled green shape indicates terms related to “capsule”.

Along with the nomenclature, reported frequencies varied, owing to different classification schemes (Figure 4), yet three major patterns emerged.

Figure 4: Reported frequencies. Frequencies of GPs by study according to consensus terms. For studies (in italics) in which a (pseudo-)capsule was assessed independently, its frequency is represented in a separate bar.