

REVIEW ARTICLE

Focal nodular hyperplasia: a review of current indications for and outcomes of hepatic resection

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Abstract

Background: Focal nodular hyperplasia (FNH) is a common benign disease of the liver with no recognized potential for malignant transformation. The term describes an entity of lobular proliferation of normally differentiated hepatocytes, frequently around a central fibrous scar. Two key issues influence surgical decision making in FNH: diagnostic certainty, and symptomatic assessment.

Methods: A systematic review of studies reporting hepatic resections of FNH was performed. Indications and outcomes in adult populations were examined with a focus on diagnostic workup, patient selection and operative mortality and morbidity.

Results: Diagnostic modalities in the majority of studies involved ultrasound and computed tomography. Fewer than half employed magnetic resonance imaging (MRI). In instances in which MRI was not available, diagnostic accuracy was inferior.

Conclusions: Percutaneous biopsy should be avoided to prevent the risk for tumour seeding. Patients presenting with asymptomatic definitive FNH can be safely managed conservatively. In symptomatic patients surgical resection is a safe and effective treatment for which acceptable rates of morbidity (14%) and zero mortality are reported. However, evidence of symptom resolution is reported with conservative strategies. Diagnostic uncertainty remains the principal valid indication for FNH resection, but only in patients in whom contrast-enhanced MRI forms part of preoperative assessment.

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Introduction

Focal nodular hyperplasia (FNH) is a common benign disease of the liver. Its incidence in females is reported to be eight times higher than in males and is weakly associated with reproductive age and use of oral contraceptives. The term describes an entity of lobular proliferation of normally differentiated hepatocytes, frequently around a central fibrovascular scar.¹ The natural history of FNH has been well studied and there is a sound evidence base for its benign classification. No instances of confirmed malignant transformation of FNH are reported in the literature.²

The profile of the typical FNH patient has changed as a result of the modern widespread availability and application of cross-sectional imaging. Previously, a significant proportion of patients diagnosed with FNH presented with vague symptoms of abdomi-

nal pain or discomfort. Such patients then proceeded to imaging and diagnosis. Today, the converse is true and the prevalent scenario concerns the incidental detection of liver lesions through high-resolution imaging performed for unrelated clinical reasons. As a result there has been broad international recognition of a substantial increase in the number of referrals for the characterization and subsequent management of suspected FNH.

There exists considerable controversy with respect to the absolute indications and contraindications for surgery in benign liver disease,³ and the available literature is unclear regarding the surgical management of FNH. The management spectrum ranges from simple observation to major hepatic resection, with two key issues influencing clinical decision making. The first is diagnostic certainty and the second symptomatic assessment. The lack of malignant potential in FNH means that when relative certainty is

achieved, the asymptomatic patient might be safely managed conservatively. However, in patients in whom indeterminate features exist, the differential diagnosis includes more concerning pathologies, such as hepatic adenoma (HA) or fibrolamellar hepatocellular carcinoma (FHCC). For such lesions resection is justified to prevent the development or under-treatment of malignancy. In symptomatic patients in whom FNH lesions are plausibly deemed to be causal, resection has been performed and reported for palliation.

This systematic review focuses on studies that report outcomes of FNH resections and give details of the preoperative diagnostic and patient selection modalities employed. Outcomes assessed are the accuracy of preoperative diagnostic investigations, stated indications for surgery, operative procedure, mortality, morbidity and patient satisfaction. Thus the indications for conservative versus surgical management of suspected FNH might be more clearly understood.

Materials and methods

Literature search strategy

A systematic review of the literature was undertaken according to the principles of the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines.⁴ No randomized studies precluding the application of relevant PRISMA items were identified.

An electronic search of the PubMed and MEDLINE databases was performed for the period 2001 to 2012 inclusive using the MeSH (medical subject headings) terms: 'focal nodular hyperplasia'; 'liver tumours'; 'liver resection', and 'hepatectomy'. The search was limited to English-language publications and studies on adult human subjects. All titles and abstracts were reviewed, and appropriate papers assessed for inclusion. The reference sections of all papers initially included were also assessed to ensure the identification of all relevant studies.

Inclusion and exclusion criteria

Studies were included if they described outcomes following hepatic resection in patients with FNH. Data collated included preoperative diagnostic methods used, indications for surgery, magnitude of hepatic resection and postoperative outcomes. The minimal dataset eligible for inclusion was required to refer to patients with FNH treated with surgery and to present diagnostic modality and patient outcome data. Series of hepatic resections for general benign disease were required to present specific FNH subgroup data. All series satisfying these criteria were included regardless of the size of the study population. Case reports, editorials, unpublished data from conference abstracts and review articles were excluded. The characteristics of excluded studies are shown in Fig. 1.

Results

Characteristics of included studies

Of the 14 studies reviewed, three focused exclusively on patients with FNH.⁵⁻⁷ Nine further studies can be described as case series of

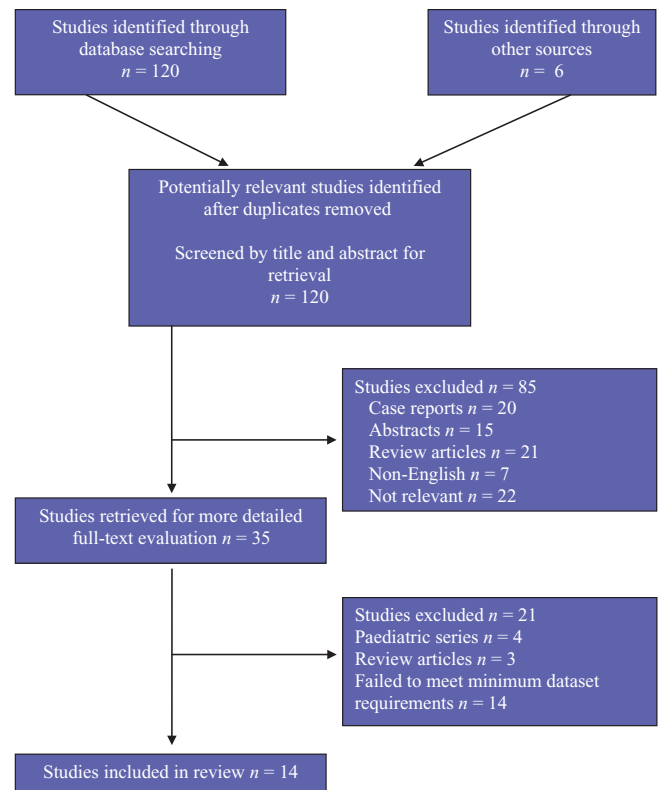


Figure 1 Flow diagram demonstrating search criteria and subsequent inclusion of relevant studies

hepatic resections performed for benign disease, including FNH.⁸⁻¹⁶ The remaining two studies reported on resections of both benign and malignant liver lesions.^{17,18} In total, the 14 studies involved 885 patients submitted to surgery for benign liver lesions, 37% ($n = 331$) of whom had a proven histological diagnosis of FNH (Table 1).

Diagnostic modalities

Seven studies provided details of the diagnostic modalities employed preoperatively in a total of 195 FNH patients.^{3-7,9,11,12,18} The reference-standard method of diagnosis of FNH is histological analysis.

Lesional biopsy

Only two studies included data on the use of biopsy in the context of the management of presumed FNH. Descottes and colleagues¹¹ reported preoperative liver investigations performed in 87 patients with benign lesions, 48 (55%) of whom were ultimately histologically diagnosed as having FNH. Within the subgroup of patients with FNH, 23% ($n = 11$) subsequently underwent either percutaneous ($n = 3$) or laparoscopic ($n = 8$) tumour biopsy. Biopsy-derived histological diagnoses were poorly correlated with resection specimen histology. Six (55%) true positive results were seen. The remaining findings included four false positive results

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