REVIEW ARTICLE

A systematic review of contralateral liver lobe hypertrophy after unilobar selective internal radiation therapy with Y90

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Abstract

Background: Curative liver resection is the treatment of choice for both primary and secondary liver malignancies. However, an inadequate future liver remnant (FLR) frequently precludes successful surgery. Portal vein embolization is the gold-standard modality for inducing hypertrophy of the FLR. In recent times, unilobar Yttrium-90 selective internal radiation therapy (SIRT) has been reported to induce hypertrophy of the contralateral, untreated liver lobe. The aim of this study is to review the current literature reporting on contralateral liver hypertrophy induced by unilobar SIRT.

Methods: A systematic review of the English-language literature between 2000 and 2014 was performed using the search terms "Yttrium 90" OR "selective internal radiation therapy" OR "radioembolization" AND "hypertrophy".

Results: Seven studies, reporting on 312 patients, were included. Two hundred and eighty four patients (91.0%) received treatment to the right lobe. Two hundred and fifteen patients had hepatocellular carcinoma (HCC), 12 had intrahepatic cholangiocarcinoma, and 85 had liver metastases from mixed primaries. Y90 SIRT resulted in contralateral liver hypertrophy which ranged from 26 to 47% at 44 days–9 months. All studies were retrospective in nature, and heterogeneous, with substantial variations relative to pathology treated, underlying liver disease, dosage and delivery of Y90, number of treatment sessions and time to measurement of hypertrophy.

Conclusion: Unilobar Y90 SIRT results in significant hypertrophy of the contralateral liver lobe. The rate of hypertrophy seems to be slower than that achieved by other methods.

Received 13 May 2015; accepted 1 July 2015

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Introduction

Liver resection (LR) with negative margins is the only potentially curative treatment in the majority of patients with both primary and secondary malignant disease.[1] However, an adequate future liver remnant (FLR) is imperative to avoid postoperative liver failure. In patients with a preserved liver function, a FLR of at least 25–30% is deemed sufficient by most clinicians to prevent liver failure.[2] However, in patients with impaired liver function (e.g. cirrhosis), a FLR of up to 40% should be preserved.[3,4] Inadequate FLR is one of the most common reasons for precluding otherwise suitable patients from potentially curative LR.

At present, the two techniques most commonly used to induce FLR hypertrophy in patients with inadequate FLR are portal vein embolization (PVE) and portal vein ligation (PVL). In head-to-head comparisons, the two techniques have been shown provide equivalent degrees of hypertrophy,[5,6] estimated to be between 10 and 46% at 2–8 weeks.[7] PVE is thus

preferentially utilised as it is minimally invasive in nature and avoids a laparotomy.

Presently, selective internal radiation therapy (SIRT) with Yttrium-90 (also known as radioembolization) has become an increasingly utilized treatment modality for locally advanced liver tumours, with radiological tumour response rates of between 42 and 70% reported.[8–10] In addition to documented efficacy for local tumour control, recent reports have described that the delivery of unilobar SIRT may result in a significant hypertrophy of the contralateral liver lobe.[11–19] This finding is relatively recent and has the potential of increasing resectability rates as it allows both tumour down-staging and induces FLR hypertrophy.

To date, there have been multiple reports—largely heterogeneous case series—describing this phenomenon. The aim of this study was to perform a systematic review of the English language literature to summarize the current evidence on liver hypertrophy following unilobar SIRT.

Methods

Systematic literature search

A systematic literature search was performed from the PubMed and Scopus databases from January 1 2000 to August 20 2014. SIRT with Y90 is a relatively new technology, and searches extending earlier than this would not yield additional results. The search terms "Yttrium 90" OR "selective internal radiation therapy" OR "radioembolization" AND "hypertrophy" were used. From the titles identified, all abstracts were screened by two authors (Teo JY and Goh BKP) to identify studies reporting on the degree of liver hypertrophy after Y90 SIRT. Subsequently, full-text articles of potentially eligible articles were screened. All references of the included studies were screened for potential relevant studies not identified by the initial literature search. The final decision on eligibility was reached by consensus between the two screening authors. There were no cases of disagreement and hence no requirement for adjudication by an independent third reviewer. When more than one study was published from the same centre, and the cohorts were overlapping, only the most recent study was included in the analysis.

Inclusion and exclusion criteria

Inclusion criteria were (i) case series reporting on $\geq$ 2 patients; (ii) undergoing unilobar SIRT with Y90 microspheres; (iii) and reporting on hypertrophy of the contralateral lobe at any time point. When volume changes at more than one independent time point were reported, the maximal volume increase was extracted and analysed.

Exclusion criteria were (i) case reports; (ii) studies which did not report volumetric changes; (iii) review articles which did not present unique data. (iv) Articles not published in English.

Data extraction

From the included studies, the following data were extracted: number of patients, pathology of disease being treated, modality and site of Y90 delivery, number of treatment sessions, method of volumetric measurement, time to determination of liver hypertrophy and degree of hypertrophy achieved.

Results

Fig. 1 shows the PRISMA flow chart for the study.[20] Nine studies, published between 2008 and 2014 were identified.[11–19] Three studies[11,12,15] were reported from the same centre with overlapping patient cohorts. Two studies[11,12] were excluded; and only the most recent (and largest) report[15] was included. Finally, 7 studies reporting on a total of 312 patients were included in the final analysis. Table 1 shows a summary of the data variables collected. All identified studies were retrospective in nature. As there was clearly a great degree of clinical heterogeneity among studies—most notably in terms of time to volumetric measurement—a meta-analysis was not performed as any result obtained would be of questionable value and difficult to interpret.

The published series were heterogeneous in terms of pathology treated, dosage and delivery of Y90, and time to measurement of hypertrophy. However, it was clear that unilobar Y90 SIRT resulted in significant hypertrophy of the contralateral lobe—the reported average hypertrophy achieved ranged from 26 to 47% over time periods of 44 days to 9 months. Of the 312 patients 284 (91.0%) received SIRT to the right lobe. In terms of underlying pathology, 215 (68.9%) patients were treated for hepatocellular carcinoma (HCC), 12 (3.8%) for intrahepatic cholangiocarcinoma and 85 (27.2%) for liver metastases from various primaries.

Comparison between SIRT and PVE

Only one study[18] attempted a direct head-to-head comparison between SIRT and PVE. Garlipp *et al.* performed a matched-pair analysis of patients with secondary liver malignancy confined to the right hemiliver. Patients were well matched for (i) baseline FLR; (ii) history of platinum-based chemotherapy; (iii) platelet count and (iv) extent of embolization. Although subject to the usual biases inherent in such a study, PVE was reported to result in significantly greater hypertrophy (PVE: 61.5%; SIRT: 29.0%) within a shorter median time frame (PVE: 33 days (range 24–56 days); SIRT: 46 days (range 27–79 days). In this study, tumour growth in both arms was not reported.

Rate of hypertrophy with SIRT

Two studies attempted to describe the time-dependant changes in liver volume.[15,17] The studies by both Vouche *et al.*[15] and Fernandez-Ros *et al.*[17] suggested that the kinetics of post-Y90 hypertrophy are slow, with gradual increases in volume, and no demonstrated plateau. However, due to differences in patient