

## ORIGINAL ARTICLE

# Angiographic identification of extrahepatic perfusion after hepatic arterial pump placement: implications for surgical prevention

Daniel R. Perez<sup>1</sup>, Nancy E. Kemeny<sup>2</sup>, Karen T. Brown<sup>3</sup>, Alexandra N. Gewirtz<sup>2</sup>, Philip B. Paty<sup>1</sup>, William R. Jarnagin<sup>1</sup> & Michael I. D'Angelica<sup>1</sup>

Departments of <sup>1</sup>Surgery, <sup>2</sup>Medical Oncology, and <sup>3</sup>Interventional Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

## Abstract

**Background:** Hepatic arterial infusion (HAI) chemotherapy is an effective treatment for patients with liver malignancy. Extrahepatic perfusion (EHP) after HAI pump placement requires correction prior to starting chemotherapy. The aim of this study was to define the origin of arterial branches causing EHP in order to determine if alterations in surgical technique during pump placement might prevent EHP.

**Methods:** A prospectively maintained, single-centre HAI database was reviewed for all patients (2008–2011) with EHP. The origin of arterial branches causing EHP was classified anatomically and patient outcomes were analysed.

**Results:** Of the 327 patients with pumps implanted, 24 evidenced EHP. The arterial branch responsible for EHP perfused the duodenum, pancreas and/or stomach. The branch responsible for EHP arose from the proper hepatic artery (PHA), 1<sup>st</sup>, 2<sup>nd</sup>, or 3<sup>rd</sup> order hepatic artery branches in 7, 10, 5 and 2 patients, respectively. The majority of branches beyond the PHA causing EHP (13/17) originated from the right hepatic artery. In 18 patients, aberrant branches were successfully treated with embolization.

**Conclusion:** These findings provide the anatomic basis for prevention of up to one-third of the cases of EHP intra-operatively, decreasing the number of patients who will require additional procedures for correction of EHP post-operatively.

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## Correspondence

Michael I. D'Angelica, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA. Tel.: +1 212 639 3226. Fax: +1 212 717 3218. E-mail: dangelim@mskcc.org

## Introduction

Hepatic artery infusion (HAI) chemotherapy for the treatment of hepatic malignancy has been studied and used for three decades in various tertiary cancer care facilities.<sup>1</sup> A Cancer and Leukemia Group B (CALGB) study of patients with unresectable metastatic colorectal cancer to the liver demonstrated increased survival, hepatic progression-free survival and response rates with HAI chemotherapy compared with systemic chemotherapy.<sup>2</sup> Three randomized clinical trials documented a disease-free survival advantage for patients with colorectal liver metastases who received a combination of HAI and systemic chemotherapy compared with systemic chemotherapy alone after liver resection.<sup>1–3</sup> Reported complications after HAI pump placement and chemotherapy treatment include hepatitis, biliary sclerosis, bleeding

and infection.<sup>3</sup> Aberrant perfusion of the non-hepatic territory, referred to herein as extrahepatic perfusion (EHP), increases toxicity and needs to be avoided or corrected before initiation of HAI chemotherapy.<sup>4–7</sup>

Surgical techniques for placement of HAI pumps in the setting of normal<sup>8</sup> and variant<sup>7</sup> hepatic arterial anatomy have been described previously. During pump placement, it is typically recommended that the common and proper hepatic arteries are circumferentially dissected 2 cm proximal and distal to the origin of the gastroduodenal artery (GDA).<sup>8</sup> Complete circumferential skeletonization of the hepatic artery and the GDA<sup>8</sup> is thus achieved and arterial branches to extrahepatic organs are ligated and divided<sup>7</sup> to eliminate the risk of EHP. Intra-operatively, EHP is assessed by injection of methylene blue (direct visualization) or fluorescein (Woods lamp visualization) via the side port of the

HAI pump catheter. The patient is reassessed post-operatively by nuclear medicine scintigraphy to rule out leakage, obstruction or EHP before starting treatment with pump chemotherapy. The organs most commonly affected by EHP include the stomach, duodenum and/or pancreas.<sup>7</sup>

Although every effort is made to ligate all extrahepatic branches during surgery, it occasionally fails or is technically not possible.<sup>7,8</sup> In spite of a negative intra-operative methylene blue or fluorescein study, nuclear scintigraphy may demonstrate EHP post-operatively. When EHP is suspected on a post-operative nuclear medicine study, patients are referred for angiographic evaluation. Once the responsible branch is identified, transcatheter embolization can be performed but in some cases is not technically possible.<sup>9</sup> The goals of this study were to define the anatomy of arterial branches causing EHP and propose surgical strategies that might minimize the risk of this complication.

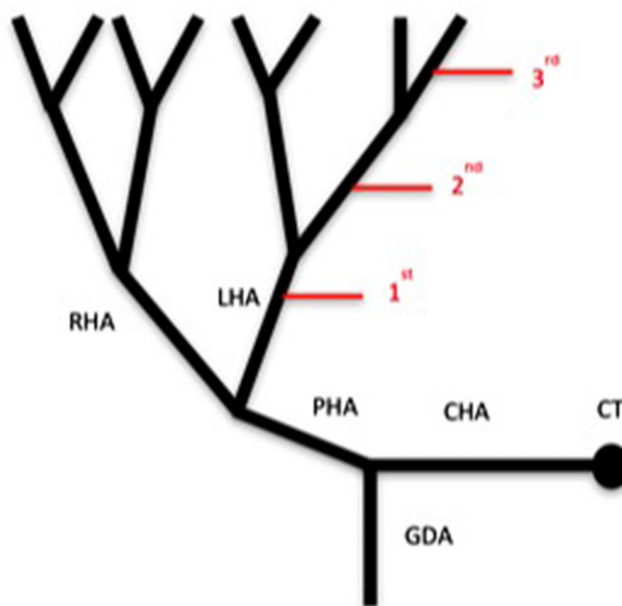
## Methods

A prospectively maintained database of patients who underwent HAI pump placement between May 2008 and May 2011 was retrospectively reviewed. The data were collected and stored in compliance with the Health Insurance Portability and Accountability Act regulations, and a waiver of authorization was obtained from the Memorial Sloan-Kettering Cancer Center Institutional Review Board to allow analysis of patient information.

Before surgery, all patients underwent computed tomographic angiography (CTA) to determine hepatic arterial anatomy. If there was evidence of EHP intra-operatively, every effort was made to identify and ligate the responsible arterial branch. In that situation, intra-operative re-testing for EHP was then performed.

In spite of meticulous surgical technique, EHP can either persist or become evident only post-operatively. Within 2 weeks of surgery, a nuclear medicine liver perfusion scan was performed with technetium 99 (<sup>99</sup>Tc) sulfur-colloid intravenously and <sup>99</sup>Tc macroaggregated albumin via the implanted pump before the device could be filled with chemotherapy. When scintigraphy showed evidence of EHP, patients were referred for angiography and embolization of responsible vessels if possible. The number of HAI pumps salvaged by arterial embolization was recorded and causes of unsuccessful embolization were analysed.

Only patients with evidence of EHP ( $n = 24$ ) on post-operative nuclear scintigraphy ( $n = 327$ ) were included in the study. The corresponding angiograms were reviewed by an experienced interventional radiologist (K.B). Vascular anatomic variations were recorded. An accessory hepatic artery was defined as a hepatic branch that originated from an artery other than the proper hepatic artery (PHA) and partially contributed to the blood supply of the hemi-liver. A replaced hepatic artery was defined similarly except that this branch completely supplied the hemi-liver. The arterial branch causing EHP was identified and its origin was determined. Branches causing EHP were divided into branches originating from the PHA or distal to the PHA bifurcation. For patients with



**Figure 1** Schematic illustration of extrahepatic branch order. 1<sup>st</sup>: first order extrahepatic branch originates either from the left (LHA) or right hepatic artery (RHA). 2<sup>nd</sup>: second order extrahepatic branch originates distal to the first branching of the RHA or LHA but proximal to the second branching of the hepatic vessels; 3<sup>rd</sup>: third order extrahepatic branch originates distal to the second branching of the hepatic vessels; PHA: proper hepatic artery; CHA: common hepatic artery; CT: celiac trunk; GDA: gastroduodenal artery

aberrant branches distal to the PHA bifurcation, the order of branching of the hepatic artery giving rise to the extrahepatic branch was determined as shown in Fig. 1. Branches originating from the right hepatic artery (RHA) or the left hepatic artery (LHA) between the bifurcation of the PHA and the first branching of the RHA or LHA were defined as 1<sup>st</sup> order. Branches arising distal to the first branching of the RHA or the LHA but proximal to the second branching of the hepatic vessels were classified as 2<sup>nd</sup> order. All branches originating distal to the second branching of the hepatic vessels were termed 3<sup>rd</sup> order branches. The distance between the tip of the HAI catheter and the origin of the aberrant vessel was estimated on angiography as either  $\leq 2$  cm or  $> 2$  cm.

## Results

HAI pumps were placed in 327 patients during the 3-year study period. Post-operatively and before using the pump, 24 (7.3%) patients had evidence of EHP on nuclear liver scintigraphy. Demographic, primary cancer diagnosis and hepatic resection data for patients with EHP are summarized in Table 1.

### Vascular anatomy and extrahepatic perfusion

Hepatic vascular anatomy data for these 24 patients with EHP is summarized in Table 2. Twenty-one of the 24 patients had

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