Original article

# The histormorphological organization of the hepato-caval interface in the human

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## Abstract

The hepatic inferior vena cava (IVC) constitutes a hemodynamically challenged zone because the vein is encased in the liver substance. This structural continuity (hepato-caval interface), may constitute adaptations to withstand increased resistance to venous return, increased blood flow due to additional blood from the liver and may afford structural support to the liver. Its structure and fiber composition, however, is little studied in humans. We used 20 fresh postmortem specimens after ethical approval. The liver and IVC were removed en block and the vein opened posteriorly by a vertical slit. Specimens were harvested with part of liver tissue from the anterior wall of the IVC. They were processed for light microscopy, and stained with Masson's Trichrome and Weigert's stains to demonstrate fibromuscular architecture and enjoining liver tissue. A characteristically thick adventitia made of collagen and elastic fibers, and longitudinal smooth muscle bundles was seen. The hepato-caval interface predominantly comprised thin bands of elastic and a few collagen fibers. A preponderance of fibers was found at the portal triads and the junctions with hepatic veins. These may comprise morphological adaptations to ensure mechanical and functional co-operation between the liver and IVC in order to counter hemodynamic challenges in the zone.

**Keywords:** hepato-caval interface, liver, histomorphology, fibers, hemodynamic challenges.

## 1 Introduction

The IVC offers support to the liver through the attachment of hepatic veins and its fibrous attachment to the liver stroma (WILLIAMS, BANISTER, BERRY et al., 1995). The hepatic portion of the IVC is the only major vein in the human body that is encased in a solid organ. Sonographic studies show that the liver surrounding the IVC changes in shape to give way for vessel capacitance (KITAMURA and KOBAYASHI, 2005). The histomorphological organization may provide the basis for these observations. Structural continuity between liver stroma and the adventitia of the HIVC has been demonstrated in dogs (MEDEIROS DE MELLO, ORSI, PIFFER et al., 2000). According to these workers, there is no potential space in the hepato-caval interface; the vessel tunica adventitia and liver parenchyma being fused via a fibrous layer. The organization of the hepato-caval interface may be relevant in the presentation of fibrotic liver disease (KITAMURA and KOBAYASHI, 2005). In spite of this, the histomorphology of the HIVC and this interface in humans is scarcely studied.

## 2 Materials

Twenty fresh autopsy specimens were obtained from the Nairobi City Mortuary after due ethical approval. The autopsy specimens were first fixed by immersion in 10% formal saline for three days. Specimens that had lasted more than 48 hours post-mortem were excluded from histology.

Serial 1 cm equidistant samples were taken from the intrahepatic (Figure 1) portion of the HIVC. The intrahepatic IVC was taken with a 2 cm block of surrounding liver tissue.

Five millimeter thick sections were selected. Fixation of the tissue was done for three days using 10% formal saline. These segments were then dehydrated in ethyl alcohol of increasing concentrations, commencing with 70% ethanol to absolute alcohol. Trichloroethane was used as a clearing agent for 1.5 hours then wax impregnation and infiltration at 60 °C for 12 hours. Sections of 7 micron thickness were cut using a Lezlar® microtome (SM2400, Germany). Dewaxing was done using xylene, and the segments were rehydrated in xylol, absolute alcohol and descending grades of alcohol up to 70% (i.e. running to water). Masson's Trichrome was used to study the cytoarchitecture and connective tissue of the IVC wall (BANCROFT and STEVENS, 1994). Weigert's and van Gieson counterstaining was used to demonstrate elastic fibers. For microscopic analysis, a Leica® light microscope (BME model, Germany) was used. The composition of elastic and collagen fibers, and the histormorphology of the surrounding hepatic substance were described, and photos taken (Olympus®, 6 megapixels).

## 3 Results

The tunica adventitia was the thickest layer of the inferior vena cava and comprised three zones. There was an innermost zone of dense fibroelastic tissue. This zone had coarse collagen transversely or obliquely oriented and in some cases condensed into bundles. Elastic fibers were thin and ran in all directions (Figure 2). A middle zone existed, consisting of longitudinally oriented smooth muscle cells bundles. These were separated by collagen septa. In some instances, elastic fibers could be seen within the smooth

muscle bundles. In some segments of the IVC, the size of the smooth muscle bundles was found to reduce outwards. The outermost zone consisted of collagen, organized in bundles, and network of longitudinally oriented elastic fibers. This zone had abundant vasa vasora, which differed in amount and diameter from segment to segment.

The hepato-caval interface was made of predominantly circular and oblique elastic fibers forming a mesh (Figure 3a). The layer adjacent to adventitia had thick longitudinally oriented elastic fibers, while that close to the liver had thin and mesh-like elastic fibers. There were collagen bundles interspersed between the elastic fibers.

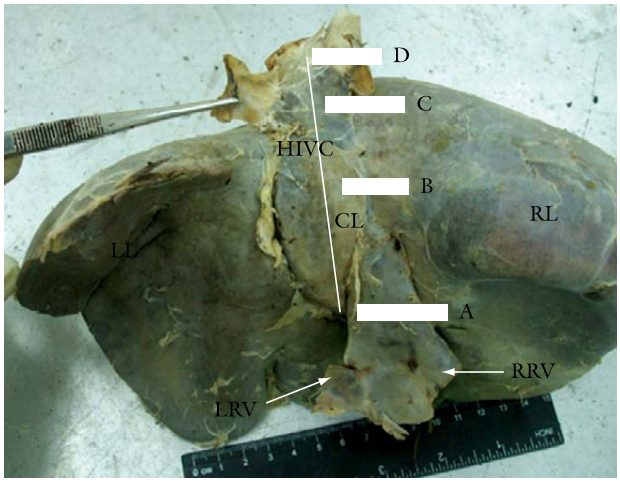


**Figure 1.** Illustration of the sampling protocol for microscopy (A-D). The near vertical line shows the extent of the IVC. CL; Caudate lobe, RL; Right lobe, RRV; Right renal vein; LRV; Left renal vein and LL; Left lobe. In this case, specimens were taken from point B on the anterior aspect of the IVC.

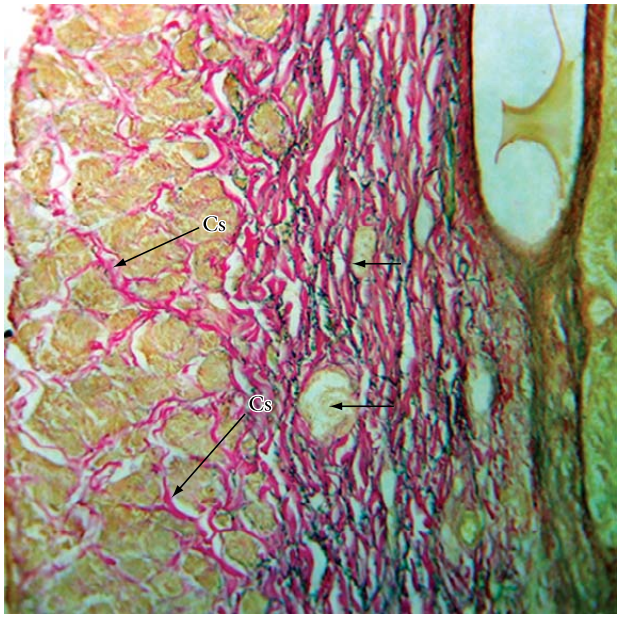


**Figure 2.** Photomicrograph of the intrahepatic IVC. Note the collagen septa (Cs) separating the muscle bundles. Numerous vasa vasora can be seen in the outer adventitia (see arrows). (Weigert elastic stain with van Gieson: ×100).

Large vascular channels were seen in the hepato-caval interface (Figure 3b). Numerous smaller vasa vasora were observed near the large channels. At junctions with hepatic veins, elastic and collagen fibers were observed to increase. The continuity presented a 'tooth-root arrangement', with two processes going deep into the liver substance and some liver tissue between them (Figure 3c). The hepato-caval interface was continuous with portal vessels through the liver parenchyma (Figure 3d).

## 4 Discussion

Our study has demonstrated that the tunica adventitia is the thickest layer in the IVC. This supports earlier findings that the tunica adventitia is the thickest layer in large veins, with predominantly longitudinal smooth muscle bundles (WHEATER, BURKITT and VICTOR, 1996). This has been observed in dogs (MEDEIROS DE MELLO, PIFFER, ORSI et al., 1997). This disposition is an adaptation for propulsion of blood against gravity (RENAUT, 1893; MEDEIROS DE MELLO, PIFFER, ORSI et al., 1997). Longitudinal muscle is absent at birth, and its occurrence is as a result of remodeling. Medial smooth muscle migrates into intima and adventitia, and become longitudinal or oblique. The forces responsible for this include hydrostatic pressure and mechanical traction due to organs (GREEP and WEISS, 1973).

Connective tissue septae were found delimiting the longitudinal smooth muscle bundles. Thick collagen fibers were found external to thin elastic fibers, which were intimately related to the smooth muscle. This was observed across the three portions of the IVC. This is akin to the spiral network of connective tissue described in the thoracic IVC of the cat and the rabbit (FRANKLIN, 1937). These, he postulated, confer strength to the IVC, which is subject to changes in length during the respiratory cycle. These connective tissue septae have also been described in the hepatic veins in man (JAMES, 1959) and hepatic portal vein (KOMURO and BURNSTOCK, 1980). Collagen may serve to protect the myo-elastic framework (KOMURO and BURNSTOCK, 1980). Networks of collagen and elastic fibers have been reported in the human inferior mesenteric vein (MEDEIROS, CARVALHO, SOUZA et al., 1988) and have been proposed to play a role in mechanochemical transduction in vessel walls (SILVER, SNOWHILL and FORAN, 2003). Existence of collagen in bundles may serve to sustain bundles of muscular fibers (CHOPARD and LUCAS, 1991).

The hepato-caval interface is the continuity between the outer adventitia of the anterior wall of IVC and the hepatic substance, and may also include the posterior wall if the IVC runs in a complete tunnel in the liver. This continuity was fibroelastic between the liver and the IVC, characterized by preponderance of elastic fibers. The elastic fibers intimately related to the liver, probably making the hepatic capsule, are thin, obliquely and circularly oriented and form a fish-net like pattern. A similar continuity has been demonstrated in dogs (MEDEIROS DE MELLO, ORSI, PIFFER et al., 2000), although connective tissue components were not elucidated. Sonographic studies also show that the IVC is closely applied to the hepatic parenchyma; hence changes in shape of the liver are accompanied by changes in caliber

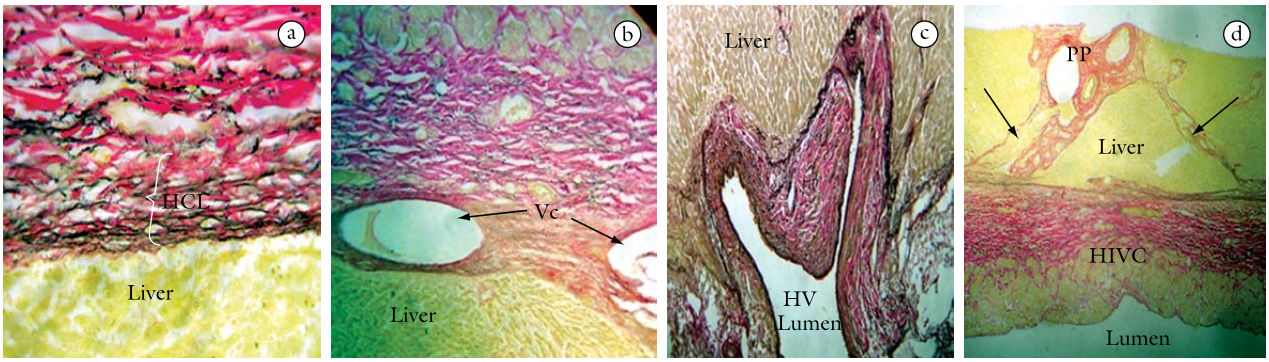


**Figure 3.** a) Photomicrograph of the intrahepatic IVC showing the hepato-caval interface (HCI). Note the thin elastic fibers adjacent to the liver and the sparse thick fibers on the adventitia. (Weigert elastic with van Gieson counterstain: ×400); b) the intrahepatic showing large vascular channels (Vc) in the hepato-caval interface. (Weigert elastic with van Gieson counterstain: ×100); c) a hepatic vein (HV) and the hepato-caval interface. Note the vein is anchored to the liver via processes. (Weigert elastic with van Gieson counterstain: ×100); d) continuity (arrows) between the hepato-caval interface and the portal pedicles (PP). (Weigert elastic with van Gieson: ×40).

of the IVC (KITAMURA and KOBAYASHI, 2005). James (1959) reported that the outermost adventitia of hepatic veins is composed of collagen and elastic fibers densely adherent to the liver. The adventitia of veins has been described as a layer of resistance against distension, sliding and length changes as well as linking to nearby structures (MOLINARI, MIRANDA NETO, CHOPARD et al., 1999). The facial vein has an elastic interface at its attachment to the submandibular gland (MOLINARI, MIRANDA NETO, CHOPARD et al., 1999). It is therefore possible that the elastic fibers demonstrated in the present study at the hepato-caval interface ensure compliance of the IVC as the liver changes shape and position during respiration.

The hepato-caval interface was observed to continue into the liver tissue and join with the connective tissue around portal pedicles. This continuity is proposed to tether the IVC into the liver. Relationship of veins with adjacent tissues by adventitial connections ensures unanimous functional system (MOLINARI, MIRANDA NETO, CHOPARD et al., 1999). This continuity of the hepato-caval into the liver may serve to reinforce the interface, therefore ensuring that the liver and IVC function unanimously. The increase in collagen on the adventitial side of the interface could serve to strengthen it, and avoid possible rupture of the IVC during extreme liver movements.

At the junction between hepatic veins and the IVC, the hepato-caval interface displayed predominance of elastic and collagen fibers, with the hepatic veins related to the liver through tooth-like processes. Previous workers have suggested that this increase in connective tissue at the junctions serves to regulate hepatic flow through a sphincteric mechanism (JAMES, 1959; FERRAZ-DE-CARVALHO, LIBERTI, FUJIMURA et al., 1994) as well as support the liver (WILLIAMS, BANISTER, BERRY et al., 1995). It is possible that this histomorphological organization constitutes an additional support mechanism to the liver.

## 5 Conclusion

We have demonstrated the morphological relationship between the inferior vena cava and the encasing hepatic substance, and it is proposed that this may be an adaptation to ensure functional co-operation to counter the increased hemodynamic stresses in this zone. Further studies to evaluate the adrenergic innervation of this region, and fine ultra-structure may shed more light.

## References

BANCROFT, JD. and STEVENS, A. Connective tissues and stains. In *Theory and practice of Histological techniques*. United Kingdom: Churchill Livingstone, 1994. p. 129-34.

CHOPARD, RP. and LUCAS, GA. Micro-mesoscopic study of fibro-muscular structures of the venous nephro-adrenal transition in humans. *Bulletin de l'Association des Anatomistes (Nancy)*, 1991, vol. 75, no. 230, p. 13-7.

FERRAZ-DE-CARVALHO, CA., LIBERTI, EA., FUJIMURA, I. and NOGUEIRA, JO. Functional anatomy of the retro-and suprahepatic portions of the human inferior vena cava and their main affluents. *Surgical and Radiological Anatomy*, 1994, vol. 16, no. 3, p. 267-75.

FRANKLIN, KJ. *A monograph on veins*. Springfield: Charles C. Thomas, 1937.

GREEP, RO. and WEISS, L. *Histology*. 3rd ed. New York: McGraw-Hill Book Company, 1973. p. 241-243.

JAMES, BG. The hepatic veins in man and their sphincter mechanisms. *Journal of Anatomy*, 1959, vol. 93, no. 3, p. 368-379.

KITAMURA, H. and KOBAYASHI, C. Impairment of change of diameter of the hepatic portion of the IVC, a sonographic sign of liver fibrosis or cirrhosis. *Journal of Ultrasound in Medicine*, 2005, vol. 24, no. 3, p. 355-359.

KOMURO, T. and BURNSTOCK, G. The fine structure of smooth muscle cells and their relationship to connective tissue in the rabbit portal vein. *Cell and Tissue Research*, 1980, vol. 210, p. 257-267.

MEDEIROS DE MELLO, J., ORSI, AM., PIFFER, CR. and TORREJAIS, MM. Architecture of the caudal vena cava wall of the dog at the level of the liver caudate lobe. *Annals of Anatomy*, 2000, vol. 182, p. 525-528.

MEDEIROS DE MELLO, J., PIFFER, CR., ORSI, AM. and ELEUTERIO, ML. Structure of the vena cava caudalis of the dog (*Canis familiaris*). *Revista Chilena de Anatomia*, 1997, vol. 15, p. 45-50.

MEDEIROS, AR., CARVALHO, CA., SOUZA, RR. and ALDO, JR. Functional anatomy of the human inferior mesenteric vein. *Anatomischer Anzeiger*, 1988, vol. 165, no. 5, p. 387-393.

MOLINARI, SL., MIRANDA NETO, MH., CHOPARD, RP. and DIDIO, LJA. Meso and microscopic study of the facial vein and adjacent tissues. *Revista Chilena de Anatomia*, 1999, vol. 17, no. 1, p. 33-37.

RENAUT, J. *Traite d'histologie pratique*. Paris: L. Battaille et Cie., 1893. Tome premier, p. 850-857.

SILVER, FH., SNOWHILL, PB. and FORAN, DJ. Mechanical behavior of vessel wall: a comparative study of aorta, vena cava and carotid artery. *Annals of Biomedical Engineering*, 2003, vol. 31, no. 7, p. 793-803.

WHEATER, RP., BURKITT, GH. and VICTOR, DG. *Wheater's functional histology*. 3rd ed. London: Churchill Livingstone, 1996. p. 151.

WILLIAMS, PL., BANISTER, LH., BERRY, MM., COLLINS, P., DYSON, M., DUSSEK, JE. and FERGUSSON, MWJ. (Ed.). Cardiovascular system. In *Gray's Anatomy*. 38th ed. London: Churchill Livingstone, 1995. p. 1451-1626.

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