

Liver Blood Flow in Man during Abdominal Surgery

II. The Effect of Hepatic Artery Occlusion on the Blood Flow through Metastatic Tumor Nodules.*

L.-E. Gelin, D. H. Lewis and L. Nilsson

Department of Surgery I (Head: L.-E. Gelin, M. D., Prof. of Surgery), Sahlgrenska
sjukhuset, Göteborg, Sweden

With the development of a method for the measurement of regional liver blood flow, as described in the previous communication, several applications, not strictly related to the original aims of the project, suggested themselves. One such, the measurement of the effect of hepatic artery occlusion on the blood flow through metastatic tumor nodules in the liver, will be reported here.

One project under study in this department is concerned with the treatment of hepatic metastases, and one therapeutic approach which is being explored is that of hepatic artery ligation. During several discussions it became apparent that the xenon method, measuring as it does flow in a small region, was ideally suited to measure blood flow in hepatic tumor nodules. Since no other technique for flow measurements in small nodules was known, and since the data could conceivably be of value at the time of operation, it was decided to conduct a series of observations. It is the purpose of this communication to describe only the results of the flow measurements in the first 3 cases studied. The theoretical basis for this form of therapy, and the follow-up of the patients will be dealt with elsewhere.

Methods and materials

The patients had all been operated upon previously for abdominal malignancy, and at the time of this study had obvious liver metastases. They were reoperated upon for the purpose of considering hepatic artery ligation as a method of treatment of the hepatic metastases, and indeed they all had livers literally full of metastases. The blood flow measurement was done by the intrahepatic injection of radioactive xenon (^{133}Xe) in saline solution, as described in the previous paper (Gelin, Lewis and Nilsson, 1967). Injections were made into normal tissue and tumor nodules on the surface of the liver, and the flow calculated from the disappearance rate of the isotope monitored externally. The two injection sites were chosen so that collimation of the detector excluded the site not being counted from the view of the detector. Observations were made before, during, and after occlusion of the hepatic artery. Where only one branch of the artery was to be occluded, care was taken to insure that the injection sites were in the area supplied by that branch. The hilus of the liver was explored thoroughly in each case to be certain that the vessel to be occluded represented the only recognizable arterial supply.

* The original research reported in this communication was made possible by the support of the United States Army through its European Research Office (Contract No. DA-91-591-EUC-3658).

Results

Fig. 1 shows the disappearance slopes of the xenon from the normal and tumor tissue, and the effect of occlusion of the hepatic artery on the flow at each site, in Case 1. In general agreement with the data from the normal patients, the effect of hepatic artery occlusion on the normal tissue was to decrease the flow to 66% of the control value. However, the flow through the tumor nodule was decreased to 8% of the control value.

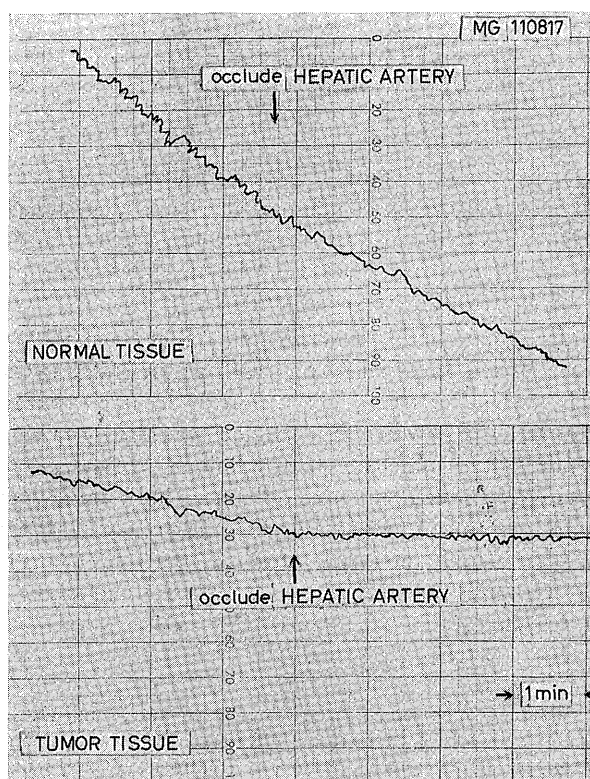


Fig. 1 (MG 110817). Effect of hepatic artery occlusion on blood flow through normal tissue (upper curve) and metastatic tumor nodule tissue (lower curve). Note that the change in the slope, i. e. reduction in blood flow is much greater with the tumor than the normal.

Table I Effect of Hepatic Artery Occlusion on Flow through Normal and Tumor Tissue.

Case	Pt.	Sex	Age	% control flow remaining after Hep. Art. Occlus.	
				Normal Tissue	Tumor Tissue
1	MG	F	53	66	8
2	SK	M	59	62	10
3	CK	M	57	19	5

This marked difference in effect was noted in the first two cases, but not in Case 3 (see Table I). It is of interest to note that in Case 3, exploration at the time of operation suggested, but did not prove, that the tumor had invaded the portal vein. The results in this case, therefore, resemble more closely those seen in the special case, described in the previous paper, with known portal vein obstruction.

Discussion

The results of this study indicate that occlusion of the hepatic artery reduces the blood flow through metastatic tumor nodules in the liver much more than in normal tissue. This is in keeping with the anatomical information that tumor nodules in the liver are supplied mainly by branches from the hepatic artery and not from the portal vein (*Breedis and Young, 1954*).

As discussed in the previous paper, the formula used to convert disappearance slope to blood flow requires knowledge of the tissue/blood partition coefficient. This is known for normal liver (*Conn, 1961*) but not, at present, for metastatic tumors. It is for this reason that the values presented have been merely the change induced by hepatic artery occlusion. It is not claimed that we know as yet the actual value for tumor blood flow.

It is not the purpose of this paper to discuss the merits of hepatic artery ligation as a form of therapy for liver metastases. That will be considered elsewhere (*Nilsson, 1966*). What should be pointed out, however, is that for whatever reason it may be desired, a method has been described for measuring blood flow in metastatic tumor nodules, or primary tumors, regardless of their size or location. The report of *Wartnaby, Bouchier, Pope, and Sherlock (1963)* deals with measurement of blood flow in a large solitary liver nodule, and it would appear that that method would have to be limited to such large nodules. To our knowledge, no other method yet described offers the possibility of measuring, at the time of operation, blood flow in tumor nodules regardless of their size. It thus promises to be of value to the surgeon by providing information not heretofore available. In the example cited in this paper, the difference in effect of hepatic artery occlusion on normal and tumor tissue was paramount in deciding to proceed with hepatic artery ligation in the first two cases, and to back off in the third.

What has been presented here can be considered as a scant beginning. The xenon method, being as it is a powerful tool, has the potential for opening up a new era in the study and treatment of metastatic tumors in man.

Summary

1. Using the intrahepatic injection of xenon as a method for the measurement of blood flow, observations were carried out on three patients with hepatic metastases.
2. It was shown that occlusion of the hepatic artery reduced tumor flow much more than flow through normal tissue. In one of the patients with probable invasion of the portal vein, the difference was not nearly as marked.
3. The xenon method originally designed for another purpose entirely has been shown capable of measuring blood flow in tumor tissue, and promises to provide the surgeon with a new and powerful tool in the study of cancer.

Zusammenfassung

1. Unter Anwendung der intrahepatischen Injektion von Xenon zur Blutstrommessung wurden Beobachtungen an 3 Patienten mit Lebermetastasen durchgeführt.
2. Es konnte gezeigt werden, daß ein Verschuß der Arteria hepatica den Blutstrom weit mehr im Tumor als im normalen Gewebe reduziert. Bei einem Patienten, bei dem wahrscheinlich eine Invasion der Vena portalis vorlag, war die Differenz nicht so stark ausgeprägt.
3. Die Xenonmethode, ursprünglich für einen anderen Zweck ausgearbeitet, hat sich als eine Methode erwiesen, mit welcher der Blutstrom im Tumorgewebe gemessen werden kann. Sie stellt eine wichtige Bereicherung im Instrumentarium des Chirurgen für das Tumorstudium (Krebsstudium) dar.

Résumé

1. Des injections intrahépatiques de xénon ont permis de mesurer le débit sanguin chez trois malades présentant des métastases hépatiques.
2. Il a été ainsi possible de démontrer qu'une oblitération de l'artère hépatique réduit le débit sanguin beaucoup plus dans la tumeur que dans le tissu intact. Chez un malade présentant probablement un envahissement de la veine porte, cette différence n'était pas aussi prononcée.
3. Cette méthode de détermination avec le xénon, conçue primordialement pour d'autres buts se révèle une technique précieuse pour déterminer le débit sanguin d'une tumeur. Elle constitue ainsi un enrichissement de valeur des méthodes chirurgicales pour l'étude des tumeurs (étude des cancers).

Resumen

1. En 3 pacientes con metástasis hepáticas se efectuaron medidas de la corriente sanguínea mediante la inyección intrahepática de xenon.
2. Se pudo demostrar que una oclusión de la arteria hepática reduce mucho más la intensidad de la corriente sanguínea en el tumor que en el tejido normal. En un paciente en que probablemente ya se había afectado la vena porta, la diferencia ya no era tan marcada.
3. El método del xenon, desarrollado originariamente con otros fines, ha resultado ser un método apto para la determinación de la irrigación sanguínea en el tejido tumoral. Es una notable contribución a los instrumentos de que dispone el cirujano para el estudio del tumor (estudio del cáncer).

Literature

- Breedis, C., G. Young: The Blood Supply of Neoplasms of the Liver. *Amer. J. Path.* 30 (1954), 969
- Conn, H. L., jr.: Equilibrium distribution of radioxenon in tissue: xenon-hemoglobin association curve. *J. Appl. Physiol.* 16 (1961), 1065
- Gelin, L.-E., D. H. Lewis, L. Nilsson: Liver Blood Flow in Man during Abdominal Surgery. I. Description of a method utilizing intrahepatic injections of radioactive xenon. Normal values and effect of temporary vascular occlusion. *Acta hepatosplen.*
- Nilsson, L. A. V.: Therapeutic Hepatic Artery Ligation in Patients with Secondary Liver Tumors. *Rev. Surg.* 23 (1966), 374
- Wartnaby, K. M., I. A. D. Bouchier, C. E. Pope II, S. Sherlock: Hepatic Blood Flow in patients with Tumors of the Liver. *Gastroenterology* 44 (1963), 733

Prof. Dr. L.-E. Gelin, Dr. D. H. Lewis, L. Nilsson, M. D. Göteborgs Universitet Medicinska Fakulteten Kir. klin. I Sahlgrenska Sjukhuset Göteborg/Schweden