Journal of Pediatric Gastroenterology and Nutrition
23:213–216 © 1996 Lippincott–Raven Publishers, Philadelphia

Medical Position Paper

Outpatient Liver Biopsy in Children: A Medical Position Statement of the North American Society for Pediatric Gastroenterology and Nutrition

Victor L. Fox, *Mitchell B. Cohen, †Peter F. Whitington, and ‡Richard B. Colletti

*Children's Hospital, Harvard Medical School, Boston, Massachusetts; *Children's Hospital, University of Cincinnati, Cincinnati, Ohio; †Wyler Children's Hospital, University of Chicago, Chicago, Illinois; and ‡Department of Pediatrics, University of Vermont College of Medicine, Burlington, Vermont, U.S.A.*

The North American Society for Pediatric Gastroenterology and Nutrition (NASPGN) recognizes the need to develop a medical position statement on percutaneous liver biopsy in infants and children to promote optimal patient care, to foster learning, and to guide practitioners, as well as to facilitate peer and other review of clinical practices. The changing healthcare environment encourages cost containment by placing greater emphasis on outpatient medical services. The outcome of diagnostic and therapeutic procedures has come under increasing scrutiny to determine which procedures may be safely and successfully conducted on an outpatient basis. Professional review organizations and medical insurance providers frequently limit reimbursement approval for percutaneous liver biopsy to an outpatient status for adult patients. The basis for this decision is published outcome data dating from 1978 to the present which demonstrate that such an approach is safe in carefully selected adult patients (1–4). Guidelines for outpatient percutaneous liver biopsy (OLB) were formulated by the Patient Care Committee of the American Gastroenterological Association and published in 1989 (5). These guidelines mention "the very young" as potentially higher risk patients who might warrant exclusion from this OLB. However, no detailed recommendations regarding appropriate selection or exclusion criteria for children were included. Pediatric gastroenterologists have continued to make decisions about percutaneous liver biopsy, including whether to perform OLB, based on limited published data and personal or anecdotal experience.

Address correspondence and reprint requests to Dr. Richard B. Colletti at A121 Given Bldg., University of Vermont, Burlington, VT 05405-0068, U.S.A.

This is a position paper authorized by the Executive Council of the North American Society for Pediatric Gastroenterology and Nutrition and is being published without editorial review.

REPORTED EXPERIENCE

Early English language reports of percutaneous liver biopsy in children described investigation of liver histology during malnutrition. In 1945, no complications associated with 92 biopsies in 45 infants and children with pellagra were reported (6). In 1949, no complications were described in 89 biopsies in 29 children aged 4–30.5 months with "nutritional dystrophy" (7). Subsequently, nine other reports published from 1955 to 1993 included 2,024 biopsies in >1,700 children (Table 1) (8–16). Other reports include very few patients or inadequate information about children in a larger adult patient series. In most studies, complication data were gathered retrospectively. The reported rates of major complications ranged from 0 to 4.5%. The incidence of postbiopsy hemorrhage requiring transfusion ranged from 0 to 2.8%. Other major complications in children, as in adults, have included pneumothorax, hemothorax, hemoperitoneum, subcapsular hematoma, bile leak, ascitic fluid leak, and pneumoscrotum (17). Three pediatric deaths have been reported.

A 1993 survey of 414 active NASPGN members (57% responding) indicated that a minority (28%) of respondents had experience with OLB in children when OLB is defined as <8-h postbiopsy monitor-

TABLE 1. *Percutaneous liver biopsy in infants and children*

Study Reference	Patients	Biopsies	Major complications	Hemorrhage	Age
Gillman and Gillman 1945 (6)	45	92	0	0	Infants, children
Meneghello et al., 1949 (7)	29	89	0	0	4–31 mo, mean 15 mo
Bruton et al., 1955 (8)	50	59	0	0	19 days to 10 yr, 22 patients ≤10 mo
Kaye et al., 1959 (9)	25	25	0	0	3 wk to 18 mo
Hong, 1960 (10)	33	36	0	0	6 wk to 12 yr, 12 patients ≤2 yr
Porter et al., 1964 (11)	36	40	0	0	2 mo to 12 yr, 17 patients <2 yr
Walker et al., 1967 (12)	166	210	1	0	1 wk to 15 yr, 67 patients ≤1 yr
Ament, 1981 (13)		584	23 (4%)		
Lichtman et al., 1987 (14)	174	184	2 (1%)	2 (1%)	All ≤1 yr, median 3 mo
Cohen et al., 1992 (15)	469		21 (4%), 3 deaths	13 (3%)	1 wk to 28 yr, median 2.6 yr
Gonzalez-Vallina et al., 1993 (16)	104	184 outpatients	0	0	5 wk to 22 yr,
		521 inpatients	5 (1%)	5 (1%)	median 7.5 yr
Total		2,024	52 (2.6%)		

ing (V. L. Fox, unpublished observations). In the only detailed series of children undergoing OLB, no significant complications were reported after 184 biopsies in 104 patients (16). More than two thirds of the biopsies were performed in patients who were recipients of a liver transplant. In the same study, 5 (1%) of 521 biopsies performed on inpatients resulted in significant hemorrhage.

The results of OLB in series of mixed pediatric and adult patients have been reported. In a series of 107 patients aged 8–73 years, 1 patient had major hemorrhage requiring surgical control (1). In another series of 829 patients aged 11–84 years, 44 (5.3%) required hospitalization for unplanned observation or treatment and 31 patients (3.6%) had major complications (2). No specific information was provided in these studies about the number of children involved or their outcome relative to the adult subjects. The complication rate of OLB in adult patients is 2.7% (range 0–3.6%) based on a cumulative total of 2,166 patients in nine separate series (4). This rate may be compared with a complication rate of 0.28% (range 0.12–0.63%) and a mortality of 0.03% (range 0–0.12%), among 189,085 adult patients undergoing inpatient liver biopsy reported in six separate studies (4). However, no prospective studies have compared the relative risk of complication from percutaneous liver biopsy in inpatients and outpatients.

The major difference between OLB and inpatient liver biopsy is the shorter period of postbiopsy observation. The safety of OLB is determined by the relative frequency of complications occurring during and after the observation period. The guidelines of the American Gastroenterological Association for adult OLB recommend at least 6 h of postbiopsy observation (5). Although most adults with significant complications manifest symptoms ≤3 h after the procedure, hypotension and death has occurred 9 h after biopsy (18) and delayed bleeding occurred 15 days after biopsy (4,19). Because few complications have been reported, very few data are available regarding the onset of signs and symptoms of hemorrhage or other major complications after liver biopsy in children. In one study, all patients who required transfusion had either a decrease in hematocrit or changes in vital signs ≤4 h after the biopsy (15). In another study, all 5 patients with hemorrhage showed signs and symptoms ≤2 h after biopsy (16). Although delayed-onset hypotension or death has not been mentioned in pediatric reports, late-onset cardiovascular instability from hypovolemic shock remains a serious concern.

Data regarding OLB in adults cannot necessarily be extrapolated to the pediatric population. Data on which to base recommendations for OLB in children are limited, and data from studies in adult patients cannot be relied on to predict outcome in children. Data from one institution may not be generalizable to others because of differences in the amount of experience, hospital resources, underlying liver diseases, and family and community support. Published experience is likely to be more favorable than experience in general, since smaller

centers and those with high rates of complications are less likely to publish their experience.

SHOCK IN INFANTS AND CHILDREN

Hemorrhage is the most important life-threatening complication of percutaneous liver biopsy, and the detection and treatment of hemorrhagic shock are critical to saving a patient's life in the event of such complication. Understanding the pathophysiology, diagnosis, and treatment of hypovolemic shock in children is therefore important when OLB is considered. The unique aspects of pediatric physiology and anatomy that place children at greater risk for hemorrhagic shock have been reviewed (20). Children have a relatively smaller total blood volume and lower hematocrit level than adults. The high ratio of body surface area to mass increases the risk of hypothermia and subsequent pulmonary hypertension, hypoxemia, and metabolic acidosis. Limited thermoregulation in infants due to inadequate subcutaneous fat and shivering mechanisms increases the risk of hypothermia and its consequences. Vital signs are age related, and early detection requires familiarity with normal values. Tachycardia is the primary response to hypovolemia in children, and children receiving β-blocking medications may be at greater risk of shock in the event of hemorrhage. In addition, gaining access to the peripheral venous system can be technically difficult.

The subtlety of early clinical signs of hypovolemic shock in infants and young children may contribute to delayed recognition and intervention as compared with the management of the condition in adult patients. Children who are uncooperative or unable to report symptoms accurately are particularly difficult to assess for early signs of shock or other complications. Cardiovascular collapse may ensue more rapidly than anticipated. No laboratory tests exist that can be used conveniently to establish the diagnosis of shock or assess acute blood volume loss accurately. Irritability and tachycardia, both early signs of hypovolemia, may be easily overlooked or misinterpreted in an active child. Cool extremities and delayed capillary refill time (>2 s) indicate serious blood volume loss of 20–25%. These signs may also be overlooked if not deliberately sought. Hypotension is a late sign of critical blood volume loss of ~40%. The problem of detection is compounded by difficulty in gaining quick access to peripheral veins for volume resuscitation of a small child or infant.

RECOMMENDATIONS

The following recommendations were prepared with the critique and endorsement of the Subcommittee on Endoscopy and Procedures, the approval of the Patient Care Committee, and the authorization of the Executive Council of NASPGN. These recommendations are subject to change based on periodic review of subsequent research.

Outpatient percutaneous liver biopsy in children and infants may be considered with the following understanding and provisions:

1. Because of potentially increased risks, and of the greater difficulty in detecting and managing shock, infants and children requiring liver biopsy should not be compelled to have liver biopsy as outpatients. However, OLB may be considered if, in the judgment of the attending physician, certain conditions are met.
2. OLB should be performed in infants and children by a physician (or under the supervision of a physician) experienced in performing the procedure in pediatric patients, only in facilities that are well equipped to provide pediatric care. Liver biopsies in infants and children should be performed only in settings that afford adequate observation and support to patients. Such a facility (a) is part of or immediately adjacent to a pediatric inpatient facility to which the patient can be admitted without delay in the event of complications; (b) has full laboratory and blood bank support; (c) has nursing personnel experienced with pediatric patients undergoing liver biopsies to observe the patient closely postbiopsy; (d) has adequate, modern equipment for constant monitoring of pulse, blood pressure, and oxygen saturation; (e) has equipment for resuscitation that is immediately available and maintained in proper working conditions.
3. OLB should not be performed in patients with an unacceptably high risk for complication. Patients with any of the following conditions may be at increased risk of either a complication or poor outcome, and hypovolemic shock after percutaneous liver biopsy may be difficult to detect in such patients: early infancy; advanced cirrhosis, ascites, or coagulopathy; coexistent major organ system disease that would imperil the patient in

the event of a complication (especially cardiac or pulmonary insufficiency); use of medications that may obscure a response to a complication (e.g., a β-receptor antagonist). Patients with underlying conditions such as, but not limited to, active malignancy (particularly hematologic or metastatic to liver), AIDS, bone marrow transplantation, and ischemic liver disease are at significantly higher risk of a complication or poor outcome after percutaneous liver biopsy and generally are not considered candidates for OLB.

4. A protocol for OLB should be established before the procedure is performed. Although routine prebiopsy testing varies among institutions, each institution should develop a consistent prebiopsy protocol, including risk assessment. OLB protocols should generally be similar to protocols for inpatients. Screening laboratory studies should include but not be limited to a complete blood count, platelet count, and coagulation studies. Intravenous access is generally maintained for patients throughout the period of postbiopsy monitoring.
5. Patients must remain at the facility for at least 6 h postbiopsy for frequent monitoring. Any evidence of hemodynamic or other instability should result in a patient's continued hospitalization until significant complications have been excluded. Before the patient is released from the facility a repeat hematocrit should be obtained and the result noted for evidence of significant occult hemorrhage. Activity should be limited for the first 24 h postbiopsy.
6. There should be a protocol for observation to detect complications that develop after the patient leaves the biopsy facility, and the patient and guardian should remain near enough to the facility to be able to return promptly. The patient's family should continue to provide adequate observation for some time after the initial 6- to 8-h period of postbiopsy observation. Children should not be considered for OLB unless they can be accompanied by a reliable guardian who will remain with them for at least 48 h postbiopsy, who can provide adequate supportive care, and who has immediate access to a telephone and transportation to the facility. In addition, in general, for the first 24 h postbiopsy, the patient and guardian should remain in the vicinity of the facility so that the patient can return quickly to the facility if a complication occurs (usually in ~30-min transportation time).
7. There should be a low threshold for use of the inpatient facility after OLB. Postbiopsy hospitalization is advised if there is evidence of significant bleeding, respiratory distress, excessive pain, prolonged sedation, other organ puncture, bile leak, or other complication.

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