Citation: Clinical and Translational Gastroenterology (2016) 7, e171; doi:10.1038/ctg.2016.30

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GUT INSTINCTS: MY PERSPECTIVE

Liver Biopsy: The Reports of Its Demise Are Greatly Exaggerated

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Clinical and Translational Gastroenterology (2016) **7,** e171; doi:10.1038/ctg.2016.30; published online 26 May 2016

I will never forget sitting in an Advisory Board meeting and watching a presentation by a well-known colleague (and proponent of one of the many alternatives to liver biopsy for fibrosis staging) showing bedside scenes from a "typical" liver biopsy which appeared as a very bloody mess, and no doubt an impressive undertaking to be avoided if at all possible especially to the non-medical Pharma advisory members. Indeed, liver biopsy always must command respect and never can be taken lightly, requiring preparation both mentally and practically for the rare but true emergency.

On the other hand, I have never seen a biopsy look quite like the one portrayed by my colleague, and one needs only to see a few remarkable misses in fibrosis staging by the "non-invasive" tests to second-guess relying on these measures routinely let alone exclusively—this is all the more true when trends become evident, such as chronically over-calling or under-calling (or helter-skelter outright missing) the fibrosis stage—all of which appear evident in various forms of non-invasive staging whether by various forms of elastography or blood profiles of collagen metabolites (anecdotal experience). Sometimes derided as a "silver standard" rather than a "gold standard", biopsy remains a foundational element of evaluating liver disease.[1]

So what does liver biopsy bring to the table? The strength of biopsy lies in its long and established history and the diversity of findings in one test especially in diagnosis as well as staging. Diagnostically, things are not always as they may seem and hence the obese, diabetic patient with abnormal liver enzymes may have findings of autoimmune hepatitis (AIH) or both steatohepatitis and AIH (anecdotal experience). Conversely, the treated AIH patient with abnormal liver enzymes could have inadequately treated AIH or with steroid induced weight gain may have transitioned to a form of fatty-liver disease. Other key histological findings, which may not always be expected, include granulomatous inflammation, evidence of bile duct injury, venous congestion, or, in the transplanted patient, evidence of rejection or inclusion bodies. Biopsy is also important in establishing tissue metal content in suspected hemochromatosis or Wilson's disease.

What are the limitations of liver biopsy? Inherent limitations have been clearly established. Much has been made of the potential for sampling error especially in fibrosis staging, but also in detection of key histological findings such as cellular ballooning in NASH.[2] This underscores the fact that biopsy is seldom a stand-alone test and optimal interpretation requires clinical context including history, laboratory values, and imaging results. It also is a reminder of the importance of technique in providing an adequate specimen. Surgical wedge biopsies, although usually providing an ample amount of tissue, are famously known to over-estimate fibrosis stage due to the proximity of the sample to the fibrous liver capsule. Core biopsies can be optimized by ensuring adequate length (>2 cm) and also the width as narrow biopsies can hamper understanding the relationship between portal tracts and central veins. Usually 15–16-gauge cores are adequate but narrower cores can be problematic. Notably, use of guidance collar on the ultrasound probe for real-time guidance can adversely influence the quality of the tissue sample when used with non-cutting, automated coring devices (such as the Biopence needle), and attention should be paid to avoiding impeding the motion of the device.

Complications of liver biopsy are uncommon but must be always vigilantly prepared for.[3] Use of ultrasound guidance either as real-time guidance or as site-marking clearly reduces inadvertent puncture of adjacent organs such as gall bladder or lung, but probably does not greatly affect the bleeding risk which depends more on transecting a small artery.[4] Serious bleeding is usually apparent in the immediate period following the biopsy. Plans for managing this uncommon complication, such as use of urgent imaging and an interventional contingency should be thought out in advance.

So where does biopsy fit into the clinical evaluation nowadays? It is clearly less important in the modern era in very straightforward cases, such as uncomplicated hepatitis C, where non-invasive tests can often serve the clinical need to help guide therapy. However, biopsy stands today where it has always been—at the foundation of clinical Hepatology. Few histological findings are genuinely pathognomonic but placed into the clinical context, the biopsy can provide invaluable information to guide optimal patient care and it serves as an important and, sometimes, definitive adjunct to the ever-growing number of non-invasive tests. It is notable that of the wide-variety of clinical trials aiming at therapeutics for NASH, involving investigators from around the world, essentially all require diagnostic entry biopsy and most require end-of-treatment biopsy for assessments of histological response.

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Two final questions can be reasonably asked. Who should perform standard percutaneous biopsies and who should interpret the biopsy? These are two important questions especially for the people putting the biopsy results into a clinical context and then acting on the results, and hence also an especially important question for the person who is undergoing the biopsy. It is human nature that the closer one is vested in an outcome, the more likely one is to take a strong interest in the outcome, especially one that can have such pivotal therapeutic implications for the patient. One has to see only a few inadequate specimens which require an "encore biopsy" to realize that the performance of liver biopsy and a more than passing familiarity with interpretation of an adequate specimen are core elements of the practice of Hepatology. Having access to a Pathologist with specialized liver training and experience is highly desirable but not always available, and thus all the more reason that training should continue to emphasize this core element of Hepatology.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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