# Transient elastography in Canada: Current state and future directions

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**BACKGROUND:** Transient elastography (TE) is a safe and effective technology to noninvasively assess hepatic fibrosis in patients with numerous liver conditions. TE is not readily available to all Canadians, and data regarding how this technology is incorporated into clinical practice are lacking.
**OBJECTIVE:** To describe TE practices in Canada, and to identify strategies to optimize access and usage.
**METHODS:** All Canadian centres with TE devices were invited to complete a survey after obtaining purchasing data from the national distributor of the device. Descriptive statistics were generated.
**RESULTS:** Forty-two devices were available in Canada as of January 2015. Seventy-one percent are used in academic settings, 74% are hospital based and 26% are in private clinics. The test is performed by trained nurses in 48% of centres, physicians in 19%, technicians in 9.5% and by any member of the health care team in 19%. Nineteen percent of centres provide satellite clinics to perform the test. While the majority of the centres perform the test at no additional cost to patients, 29% charge a variable fee.
**CONCLUSION:** In Canada, most TE devices are used in academic and/or hospital-based settings, thus limiting access to this technology to many patients. A sizeable minority of centres mandate patients pay variable out-of-pocket fees. Satellite clinics offered by some centres could increase access, but are not widespread. The lack of uniformity with TE practices in Canada suggests that a national policy is needed.

**Key Words:** *Access; Chronic liver disease; Equity; Liver fibrosis; Transient elastography*

## L'élastographie transitoire au Canada : la situation actuelle et les futures orientations

**HISTORIQUE :** L'élastographie transitoire (ÉT) est une technologie sécuritaire et efficace pour évaluer la fibrose hépatique de manière non effractive chez des patients atteints de divers problèmes hépatiques. L'ÉT n'est pas offerte à tous les Canadiens, et on ne possède pas de données sur l'intégration de cette technologie à la pratique clinique.
**OBJECTIF :** Décrire les pratiques d'ÉT au Canada et établir des stratégies pour en optimiser l'accès et l'usage.
**MÉTHODOLOGIE :** Tous les centres canadiens possédant des dispositifs d'ÉT ont été invités à participer à un sondage après avoir obtenu les données d'achat du distributeur national. Des statistiques descriptives en ont été tirées.
**RÉSULTATS :** Quarante-deux dispositifs étaient en usage au Canada en janvier 2015. De ce nombre, 71 % sont utilisés en milieu universitaire, 74 % en milieu hospitalier et 26 % dans des cliniques privées. Le test est effectué par des infirmières formées dans 48 % des centres, par des médecins dans 19 % des centres, par des techniciens dans 9,5 % des centres et par un membre de l'équipe soignante dans 19 % des centres. De plus, 19 % des centres étaient dotés de cliniques satellites pour effectuer le test. La majorité des centres effectuent le test sans frais supplémentaires pour le patient, mais 29 % demandent des sommes variables.
**CONCLUSION :** Au Canada, la plupart des dispositifs d'ÉT sont utilisés en milieu universitaire ou hospitalier, ce qui en limite l'accès pour de nombreux patients. Une minorité importante de centres exige des frais variables aux patients. Les cliniques satellites de certains centres pourraient en accroître l'accès, mais ne sont pas répandues. L'absence d'uniformité à l'égard des pratiques d'ÉT au Canada donne à penser qu'une politique nationale s'impose.

Fibrosis is an important outcome in liver diseases because it is the main contributing factor leading to cirrhosis and subsequent complications from portal hypertension. In addition to its prognostic significance, staging liver fibrosis has an important role in guiding therapy in several liver diseases. Historically, liver biopsy was the only definitive method to quantify fibrosis. Although still considered to be the gold standard, liver biopsy is an imperfect, invasive test that is associated with several inherent limitations. Aside from the potential risks of the procedure, interpretation of liver biopsy is subject to sampling error and inter/intraobserver variability among pathologists (1-3). The need for noninvasive ways to assess fibrosis has led to the development of several blood- and imaging-based tests. Although appealing to health care providers and patients, there are advantages and disadvantages to the use of such tests and, ultimately, the use of many are hindered by high cost and poor access (Table 1).

Transient elastography (TE), approved for use by Health Canada in 2009, is an effective imaging-based noninvasive technique to stage liver fibrosis in various liver conditions. The diagnostic accuracy of TE has been established in several studies. For instance, a meta-analysis of 50 studies by Friedrich-Rust et al (4) showed mean areas under the ROC curve for the diagnosis of significant fibrosis, severe fibrosis and cirrhosis of 0.84, 0.89 and 0.94, respectively (P<0.05) (4). In general, an area under the ROC curve of 1.0 is a perfect test whereas 0.5 indicates a poor test that is slightly better than random chance in predictive ability and 0.8 is considered to be a good test.

Aside from staging fibrosis, recent studies suggest prognostic significance of mean elastography measurements using TE. For example, Wang et al (5) demonstrated that a liver stiffness measurement ≥17 kPa is an independent predictor of progression of portal hypertension in patients with well compensated cirrhosis. In addition, TE can be used to monitor liver fibrosis serially over time and, when the test is performed by the patient's health care provider, results can be instantly reported to patients and immediately impact clinical management.

TE has gained wide acceptance among Canadian gastroenterologists and hepatologists. In our previous study, TE resulted in a perceived 50% reduction in the need for percutaneous liver biopsy to stage liver disease (6). Similar to our observation, Sebastiani et al (7) reported concordant results in a survey-based study of hepatologists, gastroenterologists and infectious disease specialists in Canada. Although multiple professional societies have incorporated TE in the

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**TABLE 1**
**Summary of noninvasive methods to assess hepatic fibrosis**

| Test | Description | Advantage(s) | Disadvantage(s) |
|---|---|---|---|
| **Imaging** | | | |
| Transient elastography (FibroScan, EchoSens, France) | Low-frequency and low-amplitude vibrations pass through a limited area of the liver. The wave speed measurement by pulse-echo ultrasound is converted to an estimate of elastography | 1. Easy to learn and perform<br>2. Immediate results<br>3. Moderate to high accuracy | 1. Limited availability<br>2. Reimbursment for physicians ± usually lacking<br>3. Technical difficulty in obese patients<br>4. False higher results in some circumstances |
| Magnetic resonance elastography | Low-frequency vibrations pass through the entire liver and the speed is measured by magnetic resonance imaging spin echo sequence to convert to an estimate of elastography | 1. High accuracy<br>2. Examines the entire liver<br>3. Can be used in obese patients | 1. Limited availability<br>2. High cost<br>3. Time consuming<br>4. Contraindicated in claustrophobic subjects, or iron overloaded liver |
| **Serum biomarkers** | | | |
| AST/ALT ratio (indirect marker of fibrosis) | | 1. Readily available and easy to calculate<br>2. Inexpensive | 1. Nonspecific<br>2. Poor accuracy |
| Acoustic radiation force impulse imaging (indirect marker of fibrosis) | (AST elevation*/platelet count) x 100 | 1. Readily available and easy to calculate<br>2. Inexpensive<br>3. Moderate accuracy | 1. Nonspecific<br>2. Results affected by various comorbidities |
| FibroTest (LabCorp, USA) (indirect marker of fibrosis) | Components of this mathematical calculated test include patient sex, age, gamma globulin, alpha-2-macroglobulin, haptoglobin, apolipoprotein A1 and total bilirubin levels | 1. Moderate to high accuracy to distinguish insignificant and advanced fibrosis | 1. Limited availability<br>2. Cost to laboratory or patient<br>3. False positive results in hyperbilirubinemia from any cause<br>4. Delay in test results |
| Hepascore (Quest Diagnostics, USA) (indirect marker of fibrosis) | Components of this score include patient sex, age, bilirubin, gamma-glutamyl transpeptidase, hyaluronic acid and alpha-2 macroglobulin levels | 1. Moderate to high accuracy to distinguish insignificant and advanced fibrosis | 1. Limited availability<br>2. High cost<br>3. False-positive results in hyperbilirubinemia from any cause<br>4. Delay in test results |
| FibroSpect II (*Société des Produits Nestlé SA*, Switzerland) (direct marker of fibrosis) | Components of this test include serum hyaluronic acid, tissue inhibitor of metalloproteinase-1 and alpha-2 macroglobulin levels | 1. Moderate to high accuracy to distinguish insignificant and advanced fibrosis | 1. Limited availability<br>2. Cost<br>3. Delay in test results |

**Aspartate aminotransferase (AST) level divided by the upper limit of normal for the laboratory. ALT Alanine aminotransferase*

management of viral hepatitis and other chronic liver diseases, the test remains underutilized nationally due to lack of availability and access (7,8). The goal of the present study was to describe current TE practices in Canada, and to identify strategies to optimize access and use of this technology.

## METHODS

TE device locations and clinic contact details were obtained from the national distributor of FibroScan (Echosens, France) in Canada (KNS Canada Inc) as well as publically available medical directories. All centres were contacted by telephone or fax to acquire information pertinent to TE practice, presence and number of satellite clinics covered by the same device and patient fees (if any). Descriptive statistics were generated.

## RESULTS

All 42 TE clinics were contacted between September 2014 and January 2015; of these, a response was obtained from 29 (69%) centres (Table 2). Wait times for TE only ranged from one to 52 weeks, although eight centres reported internally variable wait periods corresponding to standard duration to see the hepatologist or gastroenterologist. Provincial distribution of the devices is shown in Table 3. Thirty-six of the nation's 42 devices are in the provinces of Ontario (n=13 [31%]), Quebec (n=9 [21%]), British Columbia (n=8 [19%]) and Alberta (n=6 [14%]). Seventy-four percent (n=31) of devices are in hospital settings, including 71% (n=30) in University centres and the remaining 26% (n=11) in privatized clinics. Six centres (21% of respondent clinics) charged patients a fee for the test, ranging from $80 to $125, whereas 79% performed the test at no additional cost to patients. Sixty percent of centres reported results immediately to patients after completion of TE and 40% of surveyed centres provide results to referring physicians only. Of respondent centres, TE was in use for a mean of 3.5 days per week (range one to five days (Table 2).

## DISCUSSION

TE is a novel technology that can play an important role in the noninvasive assessment of liver fibrosis, which is essential to the management of patients with chronic liver diseases. The present study revealed that there are only 42 devices confined to Canada's largest cities – a miniscule number considering the national burden of liver disease and generally lengthy wait times reported as the standard waitlist period with the hepatologist/gastroenterologist who would conduct the test as part of a routine consultation, to approximately one year for TE test alone in Nova Scotia. These data, in conjunction with previous published studies, demonstrates abysmal access to TE and the resultant previously reported underutilization of the test is, thus, not surprising.

Barriers, in fact, exist at multiple levels that impact the use of TE in Canada. It is possible to categorize these barriers at the system, practitioner and patient level to facilitate further analysis. At the system level, the limited availability of the technology requires improved integration among external community-based treatment settings.

**TABLE 2**
**Summary of survey results**

| Transient elastography variable | |
|---|---|
| Device setting | |
| Academic/community | 30 (71)/12 (29) |
| Hospital/private clinic | 31 (74)/11 (26) |
| Response rate (n=42 centres) | 29 (69) |
| Satellite clinics offered | |
| Yes | 6 (20.7) |
| No | 23 (79.3) |
| Primary operator | |
| Nurse | 17 (59) |
| Physician | 5 (17) |
| Technician | 2 (7) |
| Any of the above | 5 (17) |
| Wait time, weeks, mean (range) | 5.7 (1–52) |
| Usage, days/week, mean (range) | 3.5 (1–5) |
| Fee for patient | |
| Yes | 6 (20.7) |
| No | 23 (79.3) |
| Results given to: % | |
| Patient ± referring physician | 60 |
| Referring physician only | 40 |

*Data presented as n (%) unless otherwise indicated*

Successful use of this technology, therefore, necessitates a revision of community-based models of care that integrate assertive engagement and shared utilization of limited resources. Additionally, current reimbursement policies serve as a systemic barrier to widespread use of this technology. In France, *la Haute Authorité de Santé* has approved reimbursement for TE and FibroTest (LabCorp, USA) since 2007, while in Canada, TE is currently reimbursed only in Quebec (7). The implications of no physician reimbursement for TE across Canada's remaining nine provinces renders acquisition and maintenance of a TE device financially unfeasible for many practitioners, especially considering that initial costs of current models are approximately $100,000.

At the practitioner level, there are significant hindrances to the use of this technology. First, wait times and the lack of local devices render widespread, routine use problematic. Furthermore, a nationwide Canadian survey revealed that individual physician characteristics impact their willingness to use TE (7). For instance, Sebastiani et al (7) showed that older physicians used more noninvasive methods for liver fibrosis than younger respondents (P=0.02). Interestingly, hepatologists and infectious diseases specialists used more noninvasive methods for liver fibrosis (particularly TE) than gastroenterologists, although this difference was not statistically significant. The results of the current study showed remarkable variability in practice patterns and access to TE among the various provinces and in urban versus rural settings. In addition to the limited number of devices available in Canada, the devices are mainly located in tertiary liver centres and selected private clinics in densely populated urban areas. While satellite clinics may help to address the lack of availability of TE in lower-density populations and reduced wait times for patients within and outside of urban areas, only six centres (14% of respondent centres) in Canada are performing TE in secondary locations. Clearly, there may be logistic barriers to operating satellite clinics not addressed in the present study, including the fear of damage to the equipment in transport, lack of available trained personnel and lack of external resources to support such endeavours.

At the patient level, the primary barriers to the routine use of TE in Canada are limited access and variable costs associated with access. Inasmuch as all these factors play significant roles in serving as barriers to TE use, the limited availability of the technology is perhaps the most significant. As of January 2015, approximately 70% Canada's 42 devices are located in three provinces, while more than one-half

**TABLE 3**
**Distribution of FibroScan (Echosens, France) devices according to province and city in Canada (n=42)**

| Province | FibroScan devices, n |
|---|---|
| Ontario (n=13 [31%]) | |
| Toronto | 6 |
| Ottawa | 2 |
| Hamilton | 2 |
| London | 1 |
| Brampton | 1 |
| Sudbury | 1 |
| Quebec (n=9 [21.4%]) | |
| Montreal | 6 |
| Quebec city | 2 |
| Saint-Hyacinthe | 1 |
| British Columbia (n=8 [19%]) | |
| Vancouver | 5 |
| Victoria | 1 |
| Prince George | 1 |
| Kelowna | 1 |
| Alberta (n=6 [14.3%]) | |
| Edmonton | 3 |
| Calgary | 3 |
| Saskatchewan (n=3 [7%]) | |
| Saskatoon | 2 |
| Regina | 1 |
| Nova Scotia (n=1 [2.4%]) | |
| Halifax | 1 |
| New Brunswick (n=1 [2.4%]) | |
| Moncton | 1 |
| Manitoba (n=1 [2.4%]) | |
| Winnipeg | 1 |

**TABLE 4**
**Per capita availability of FibroScan (Echosens, France) according to Canadian province**

| Province | FibroScan devices, n | Population, $\times 10^6$ | Per capita availability |
|---|---|---|---|
| Ontario | 13 | 13.6 | 0.96 |
| Quebec | 9 | 8.2 | 1.10 |
| British Columbia | 8 | 4.6 | 1.74 |
| Alberta | 6 | 4.1 | 1.46 |
| Saskatchewan | 3 | 1.1 | 2.73 |
| Manitoba | 1 | 1.3 | 0.77 |
| Nova Scotia | 1 | 0.9 | 1.11 |
| New Brunswick | 1 | 0.8 | 1.25 |
| Newfoundland | 0 | 0.5 | 0 |

are in the five largest cities. Although a population-based argument can be made for even more TE devices in these cities, the current distribution leaves a considerable geographical area with no access to TE. A comparison of the per capita availability of FibroScan according to province is presented in Table 4.

Few (11 of 42 [26%]) of the devices are located in private clinics while the majority are situated within hospitals. To improve access to TE, 21% (six of 29) the respondent centres offer satellite clinics for the test where one machine is transported to offsite locations. Of the respondent centres, 7% (two of 29) are private clinics dedicated solely to perform TE for referring physicians while 55% (16 of 29) perform TE as part of a standard patient assessment. Dedicated TE clinics may conceivably help minimize wait times and improve test access, although this

remains to be proven at the patient level because patients will presumably wait additional time to obtain follow-up with their referring physicians. Direct and indirect costs to patients for TE is another likely impediment. Our results indicate that nearly 21% of centres charge patients an out-of-pocket fee for test completion (range $80 to $125). While approximately 75% of patient respondents in a survey published by Kan et al (9) expressed a willingness to pay for TE, indirect costs, such as transportation, parking, time away from work, etc, likely contribute significantly to overall patient-associated costs. Given Canada's single-tier heath care system with central principles of equity and accessibility, a broader question regarding lack of universal coverage for a medically necessary test and fairness in variability of direct costs requires further consideration, especially given that many patients with chronic liver diseases have low socioeconomic backgrounds.

From a financial prospective, a cost analysis study from the United States published in 2000 (10) showed that performing percutaneous liver biopsy with no complication costs US$1,033 per patient, which is highly comparable with the cost in Canada. In the case of a complication of liver biopsy requiring hospitalization, the median direct cost can reach $4,579 according to a 2008 Canadian population-based study (11). Because liver fibrosis is a dynamic process, significant proportions of patients require surveillance assessment of fibrosis stage in periodic intervals, which adds to total cost, and renders liver biopsy a poor diagnostic option from the patient and provider perspective. On the other hand, the cost of purchasing a current model of the TE device with a variable yearly maintenance fee is approximately $100,000. This amount would suggest TE would be revenue neutral once it is used appropriately in lieu of percutaneous liver biopsy in just 100 patients. It follows that in a British cost-effectiveness analysis, TE was more cost effective than percutaneous liver biopsy in an economic model involving 1000 patients (12).

Aside from the cost benefits and clear clinical utility of TE, Kan et al (9) demonstrated that patients strongly favour TE for the assessment of liver fibrosis. In that study, questionnaires were distributed to patients who had and had not previously undergone percutaneous liver biopsies to evaluate patient preference for TE versus liver biopsy, and to assess the willingness to self-pay for TE. Overall, an astounding 95.4% of patients preferred TE to percutaneous liver biopsy, citing benefits of improved comfort and short duration to receive results. These results, coupled with our findings, further support the need for systemic policy change at the provincial level to facilitate patient access to TE.

In Canada, liver disease is associated with significant personal and health care costs, and current mortality rates are largely underestimated, in part due to variance in reporting and inaccurate *International Classification of Diseases* coding (13). The staging of liver fibrosis is the single most important factor impacting the prognosis of patients with chronic liver diseases and it has a major role in management decisions. Inasmuch as there is a clear need for early diagnosis and staging of liver fibrosis, in 20% of patients with chronic liver diseases, the diagnosis of cirrhosis is made on presentation of the first episode of hepatic decompensation (14). Hence, the effective implementation of noninvasive liver fibrosis staging, such as via TE technology, will enable preclinical management and will facilitate effective long-term planning for these patients.

Another issue that will impact the widespread availability of TE in Canada may be competition with radiologists for newer technologies that will assess elastography using currently available magnetic resonce imaging or ultrasound systems. However, the advent of new radiological technologies, such as acoustic radiation force impulse imaging, creates an opportunity for interdisciplinary collaboration in the noninvasive assessment of liver disease. Our study highlights that there are significant barriers to widespread use of this technology within Canada, and hopefully serves as the nidus for spearheading effective policy changes at the provincial levels to render it more accessible.

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