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ORIGINAL RESEARCH

Outcomes of National Survey of the Practice of Hepatocellular Carcinoma Surveillance

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Background & Aim: HCC has significantly improved outcomes when detected early. Guidelines recommend biannual surveillance with ultrasound (US) and/or AFP in at-risk individuals. This survey aimed to describe HCC surveillance adherence/practices amongst the NHS hospitals in the UK.

Methods: An electronic survey was sent to 79 NHS hospitals via the British Association for the Study of the Liver distribution list. The responses were captured from July 2021 to January 2022. Centres were divided into hepato-pancreato-biliary (HPB) and non-HPB centres, depending on whether the hospital undertakes major liver surgeries.

Results: A total of 39 (49.3%) centres responded: 15 HPB and 24 non-HPB centres from across the UK. HCC surveillance eligibility criteria were universally applied, but heterogeneous approaches occur outside these criteria. Eighty per cent of patients undergoing surveillance were estimated to have cirrhosis. Eighty-five per cent of centres do 6-monthly US and AFP requested by clinicians and liver clinical nurse specialists. Compliance was estimated at 80% but not routinely audited. In most centres, general sonographers and/or radiologists perform surveillance US scans without a standard reporting template, although structured reporting was viewed as desirable by the majority. Poor views on US are approached heterogeneously, with patients variably offered ongoing US, CT, or MRI with different protocols.

Conclusion: Most responding NHS hospitals follow 6-monthly HCC surveillance guidance. Data recording is variable, with limited routine data collection regarding compliance, yield, and quality. Surveillance US is mostly performed by non-HPB specialists without standardised reporting. There is an inconsistent approach to poor views with US surveillance. Even in a universal healthcare system such as NHS, which is free at the point of care, delivery of HCC surveillance has not improved over the last decade and remains variable.

Keywords: hepatocellular carcinoma, primary surveillance, ultrasound scan, cirrhosis, liver cancer

Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and accounts for 75–90% of liver cancers.[1] It is a major global health problem. HCC accounts for 854,000 new cases and 810,000 deaths per year globally.[2] It is the fifth most common cancer and the second leading cause of cancer-related deaths worldwide.[3] In 2020, HCC was in the top three causes of cancer-related deaths in 46 countries and in the top five causes of cancer-related deaths in 90 countries worldwide.[4] By 2040 the number of new cases and deaths from HCC is predicted to rise by more than 55%.[4] Furthermore, survival of patients with early-stage HCC is significantly higher, at least in part due to the availability of curative treatment options, compared to those with intermediate and advanced-stage HCC.[5]

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The increasing incidence of HCC and the availability of curative treatment mandates the diagnosis of HCC in early stages. Thus, all international guidelines recommend that at-risk patients such as those with cirrhosis or chronic hepatitis B infection undergo 6-monthly ultrasound (US) ± α-fetoprotein (AFP) for primary surveillance.[6–10] Primary HCC surveillance has been shown to improve early-stage detection of HCC, leading to receipt of curative treatment and improved survival.[11] However, provision of primary HCC surveillance service is highly variable, with fewer than expected patients undergoing surveillance.[12–14] In addition, there appears to be a lack of standardisation of eligibility for primary surveillance, implementation of primary surveillance protocols, quality control of surveillance, reporting procedures, and audit of patient outcomes and service utilisation.

This study aims to survey the practice of primary HCC surveillance amongst the National Health Service (NHS) hospitals in the United Kingdom (UK).

Methods

An electronic survey was conducted through a series of questions that were reviewed and approved by the authors (Supplementary Materials). The electronic survey was distributed to 79 NHS hospitals via the British Association for the Study of the Liver (BASL) email distribution list. The survey required a single response per centre from the Head of Service or the HCC Lead Clinician in order to prevent duplication of responses and to understand the policy of each NHS hospital and not the individual clinician, and thereby overcome individual practice bias and give the best and most accurate reflection of the current clinical service offered. Survey domains included centre details and eligibility for HCC surveillance, provision of HCC surveillance service, and provision of HCC surveillance imaging. The responses were captured from July 2021 to January 2022. As this was a national survey of HCC surveillance provision without any information of individual patients, it did not require ethical approval.

Analysis

Centres were divided into two groups – hepato-pancreato-biliary (HPB) centres, defined as those that undertake major liver surgeries such as liver resections, and non-HPB centres. Liver transplant centres were included in HPB centres for analysis.

Categorical variables were presented as number with percentages rounded to the nearest integer (if applicable). Continuous variables were presented as median and range. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (Armonk, NY) or GraphPad prism 9 (San Diego, CA). Mann–Whitney and chi-square tests were used as appropriate to compare data. A p-value of <0.05 was considered significant.

Results

Centres Which Responded

Thirty-nine of 79 (49.3%) centres responded to the survey – 15 HPB centres (including six liver transplant centres) and 24 non-HPB centres from across the UK. (Figure 1).

Overall, each centre had a median of 5 (range 2–19) consultants involved in the management of patients with chronic liver disease (CLD). Ninety per cent (n=35) of centres had a lead consultant for HCC surveillance. Overall, each centre had a median of 3 (range 2–19) clinical nurse specialists (CNS) to support the hepatology service, and 67% (n=26) had a lead CNS for hepatology. Eighteen per cent (n=7) of the centres had at least level 1 accreditation of Improving Quality in Liver Services (IQILS), a Royal College of Physicians' accreditation process of evaluating the quality of clinical services against established standards. Thirty-three per cent (n=13) of centres maintained a database of patients with CLD.

HPB centres (n=15) were better staffed with more consultants (median 8 vs 4; p=0.03). However, there was no statistically significant difference in the number of clinical specialist nurses (median 2 vs 1.5; p=0.12) involved in the care of patients with CLD and HCC surveillance between HPB and non-HPB centres (n=24). The number of patients with CLD cared for was higher only numerically in HPB centres than in non-HPB centres (median 1250 vs 500, respectively; p=0.38), but the number of patients to consultant ratio (median 156 vs 145; p=0.89) and patients to CNS ratio (median 140 vs 233; p=0.20) were similar between the HPB and non-HPB centres (Table 1).

Figure 1 NHS Trusts in the UK that responded to the electronic survey. Centres are colour coded according to the number of patients reported to be under primary hepatocellular carcinoma (HCC surveillance).

Surveillance Programme

Ninety-two per cent (*n*=36) of the centres reported having an established HCC surveillance programme, co-ordinated by a median of 4.5 (range 1–19) consultants, supported by a median of 2 (range 0–10) CNSs. However, only 8% (*n*=3) had dedicated administrative support for the delivery of their HCC surveillance programme; 36% (*n*=14) had a written standard operating procedure to detail which patients should enter the HCC surveillance programme.

HCC surveillance eligibility criteria were universally applied to all Child–Pugh A, B, and C (if listed for or eligible for liver transplantation) patients, and all patients with chronic hepatitis B virus (HBV) infection and significant fibrosis, by all centres. Outside these criteria, however, eligibility criteria for HCC surveillance were very variable and heterogeneous. Some centres included all Child–Pugh stage C patients or all patients with HBV or autoimmune liver disease, primary biliary cholangitis, primary sclerosing cholangitis, or haemochromatosis, or chronic hepatitis C virus (HCV) infection, or patients with non-alcoholic fatty liver disease (NAFLD) and F3 fibrosis, or a family history of HCC. As an

Table 1 Comparison Between HPB Centres and Non-HPB Centres

	All (*n*=39) Median (Range)	HPB Centres (*n*=15) Median (Range)	Non-HPB Centres (*n*=24) Median (Range)	*p* value
Number of consultants	5 (2–19)	8 (3–15)	4 (1–15)	0.03
Number of CNS	3 (0–13)	2 (0–10)	1.5 (0–5)	0.12
Patients on HCC surveillance	700 (100–3000)	1250 (300–3000)	500 (100–1250)	0.38
Patient/consultant ratio	150 (28–750)	156 (27–750)	145 (43–500)	0.89
Patient/CNS ratio	150 (83–1500)	140 (60–1500)	233 (54–1250)	0.20

Abbreviations: CNS, clinical nurse specialists; HCC, hepatocellular carcinoma; HPB, hepato-pancreato-biliary.

example of the variation in practice, several centres reported offering surveillance to patients with PSC (*n*=17, 44%), PBC (*n*=10, 26%), and AIH (*n*=8, 21%), with only a small number (*n*=5, 13%) qualifying that HCC screening was exclusively offered to those with advanced fibrosis.

When patients entered the HCC surveillance programme, most centres offered them either verbal (46%, *n*=18) or verbal combined with written (46%, *n*=18) information. A minority of centres (8%, *n*=3) centres reported not providing formal verbal or written information to patients about their HCC surveillance programme.

Surveillance Practices

Centres estimated a median of 700 (range 100–3000) patients to undergo HCC surveillance regularly. An estimated 80% (range 70–90%) of patients undergoing HCC surveillance had cirrhosis. A total of 82% (*n*=32) of centres report undertaking both US scan and serum AFP every six months, while the remaining 18% (*n*=7) only offered biannual US scan. Only 13% (*n*=5) of centres undertook a regular audit of their HCC surveillance programme. The HCC surveillance requests were made by clinicians and CNSs in all centres; radiologists or sonographers were not involved in requesting surveillance scan requests.

Quality of Surveillance

Compliance was estimated at 80% (range 70–90%) but was not routinely audited – 26% (*n*=10) of centres were unsure of their compliance rates. In 79% (*n*=31) centres general sonographers or radiologists performed the surveillance US scans. In 21% (*n*=8) centres, surveillance US scans were exclusively performed by a subset of sonographers or radiologists with specialist knowledge of liver disease. A standardised reporting template for surveillance US scan reporting was not used in 79% (*n*=31) centres but was in place in 21% (*n*=8) of centres. However, using a structured reporting template was viewed as desirable by most centres (79%, *n*=31). In 87% (*n*=34) of centres, advice for the clinical team to arrange additional diagnostic scans accompanied an abnormal surveillance US scan as routine, while 10% (*n*=4) reported no such written advice from the radiology team undertaking the surveillance US scan. In a single centre (3%) subsequent diagnostic scans were automatically arranged by the radiology team following an abnormal surveillance US scan.

Approach to Poor US Scan Visualisation

Poor views on US scans were approached heterogeneously: 28% (*n*=11) of centres had an agreed pathway for patients with suboptimal surveillance US views; the rest (72%, *n*=28) did not have a pre-agreed pathway in place. Most centres (95%, *n*=37) indicated that they would offer an alternative surveillance test, which included ongoing US scans (18%, *n*=7), CT or MRI (77%, *n*=30), with a range of different protocols. CT or MRI was offered in 62% (*n*=24) centres as primary surveillance modality, to "high-risk" patients with compromised surveillance US views. Some centres (51%, *n*=20) offered CT or MRI to all "high-risk" patients. A few centres (10%, *n*=4) only instigated CT or MRI surveillance after recommendation from multidisciplinary team (MDT) meetings.

Discussion

This study details difference in HCC surveillance offered by 39 NHS hospitals across the UK. Most responding UK NHS hospitals follow 6-monthly surveillance guidance for primary HCC surveillance as recommended by the National Institute for Health and Care Excellence (NICE). However, data recording of HCC surveillance practice was highly variable with limited routine data collection on compliance rate, yield rate, and quality of surveillance scans. HCC surveillance US scans were mostly performed by non-specialists, no standardised reporting. There was an inconsistent approach to poor surveillance US views.

Broadly, the results of this study show that there has been little improvement in HCC surveillance over the past decade (summarised in Table 2).[14] There were similar numbers of clinicians within each centre, with services predominantly delivered on an ad hoc basis. There seems to be an improvement in information given prior to enrolment into a surveillance programme from 71.5% in 2015 to 92% in the present study, albeit mostly verbal. Surveillance US scans continue to be performed predominantly by non-specialists. Patient selection remains heterogeneous outside guideline criteria.

This survey was undertaken in collaboration with BASL, which represents hepatologists in the UK and the British Society of Gastrointestinal and Abdominal Radiology (BSGAR), which represents hepato-pancreato-biliary (HPB) radiologists in the UK. Involvement of these societies in this study could potentially lead to some easy wins to drive up the standard of HCC surveillance by establishing standardised pathways and protocols to navigate difficult territories such as managing patients with poor surveillance US views. Historically, HCC was driven by cirrhosis secondary to chronic HCV, but in the era of direct-acting antivirals (DAA), which effectively offers a cure for almost all chronic HCV cases, HCC is increasingly being driven by rising rates of NAFLD in the context of obesity and metabolic syndrome.[15,16] US scan visualisation has been shown to be inadequate in as high as 20% of obese patients undergoing HCC surveillance.[17] In this study, there was almost an equal split in opinion for offering CT or MRI vs US for primary surveillance especially in patients deemed "high risk" for HCC, albeit "high risk" has not been defined universally. This study highlights the desperate need for investment in evidence-based standardisation of services and studies into cost-effectiveness for these groups. HCC surveillance is uniquely poorly resourced compared to other national cancer screening programmes such as breast, cervical, and bowel cancer screening in terms of infrastructure, audit data, quality assurance, national standards, pathways, and evidence base.

Lack of good data is hampering high-quality cost-effective service delivery that is standardised across the country. The IQILS programme was launched in 2017 to improve the quality of medical liver services throughout the UK by the Royal College of Physicians, supported by BASL and British Society of Gastroenterology (BSG). Future quality indicators could include accurate recording of HCC surveillance data and may help to drive up the quality of service delivery and data recording. More robust data may also help build a case to invest in research strategies and lobby for

Table 2 Comparison Between HCC Surveillance Practice in 2014[14] and in 2021 (Current Study)

	2014	2021
Centres responded	84%	49%
Proportion of non-HPB centres	58%	62%
Consultant staffing (median, range)	4 (1–10)	5 (2–19)
Centres with an established US HCC surveillance programme	97%	92%
Verbal/written explanation given to patient	71%	92%
Non-specialist radiographers/radiologists performing surveillance scans	77%	79%
Automatic request of additional diagnostic scan if abnormality detected	9%	3%
Regular audit of HCC surveillance programme	8%	13%

Abbreviations: HCC, hepatocellular carcinoma; HPB, hepato-pancreato-biliary; US, ultrasound scan.

national infrastructure to start to compile data on standards and evidence-based, cost-effective pathways. With increasing prevalence of obesity and NAFLD, and their impact on US scan visualisation adequacy, there is an urgent need to standardise approaches to suboptimal surveillance US scans. One approach could be to adopt the Ultrasound Liver Imaging Reporting and Data System (US LI-RADS) algorithm.[18]

This study has its own strengths and weaknesses. This survey reports a snapshot of UK HCC surveillance practices across a variety of settings from liver transplant centres to non-HPB centres. However, there is likely to be a strong responder reporting bias from the centres particularly interested in HCC surveillance, with over-representation by BASL members and under-representation from non-members. Thus, the results presented in this study likely reflect an over-estimate of HCC surveillance practice across the UK weighted by interested centres. Moreover, in the absence of national databases, the data of this study are from estimates by the lead clinicians, which is subject to personal bias. In addition, this study did not explore the barriers to the implementation of robust HCC surveillance, which should be considered a major limitation.

In conclusion, most responding UK NHS hospitals follow 6-monthly surveillance guidance from primary HCC surveillance. Data recording of HCC surveillance practice was variable with limited routine data collection practice with regard to compliance, yield, and quality. HCC surveillance US is mostly performed by non-HPB specialists without standardised reporting. There appears to be an inconsistent approach to poor views with surveillance US scans, highlighting a need for standardised protocols in appropriate patients where visualisation is inadequate, for example the use of non-contrast abbreviated MRI.[19] The quality of HCC screening may be improved by consistent resourcing and standardised pathways, data collection, and quality assurance.

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Disclosure

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