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Is It Feasible to Apply Preference-Based Quality-of-Life Measures on Patients with Chronic Myeloid Leukemia?

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Abstract

Chronic myeloid leukemia (CML) has become a chronic and costly disease, since the launch and long-term use of tyrosine kinase inhibitors, including imatinib. Evidence for imatinib's cost-effectiveness impact were largely based on preference-based quality of life (QoL) measured from randomized controlled trials, however, little is known about the feasibility of QoL measured as a follow-up indicator in real life. This commentary describes our experiences in exploring the QoL measures and attributes influencing QoL in Taiwanese CML patients who were receiving imatinib treatment.

Keywords: Chronic myeloid leukemia; quality-of-life; EuroQol group 5-dimension; EQ-5D visual analogue scale; Time-trade off; Face-to-face interview survey; Taiwan

Abbreviations

CML: Chronic Myeloid Leukemia; Qol: Quality-of-Life; EQ-5D: Euroqol Group 5-Dimension; EQ-VAS: EQ-5D Visual Analogue Scale; TTO: Time-Trade Off; BCR: Breakpoint Cluster Region; ABL: Abelson

Introduction

The launch of Imatinib, a tyrosine kinase inhibitor, in the last decade, it has turned chronic myeloid leukemia (CML) from a progressive and fatal disease into a chronic condition. Imatinib has become the first-line therapy of CML due to the marked benefit in prolong survival [1], mild adverse effects and convenient administration rout. However, the long-term use of expensive Imatinib causes increasing healthcare burden and CML has become one of the most costly diseases [2]. The decision on whether and how to sustain the long-term, expensive cancer treatments is a challenging issue to most healthcare providers and payers.

The cost-effectiveness evidence of imatinib was largely based on phase III randomized controlled trials which only included chronic phase CML patients, followed less than 18 months [3], and used the preference-based utility measure which is based on quality-of-life (QoL) measure, such as EuroQol group 5-dimension (EQ-5D) measure. In clinical practice, clinical biomarkers and prolong survival years are routinely used in treatment and follow-up decision, but the role of utility measure is still unclear.

In addition, results of QoL measure may vary by different individual characteristics, disease conditions and cultural contexts, as QoL is defined by the World Health Organization as "the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [4]. Therefore, to evaluate the appropriateness of applying QoL measures, the underlying attributes to QoL for CML patients and patients' special concerns with Imatinib in relation to QoL should be explored.

To understand CML patients' perceptions about the QoL measures and explore underlying attributes to QoL for CML patients, we conducted a feasibility study that usedEQ-5D index and time-trade off (TTO) method to evaluate the utility for CML outpatients treated with imatinib in Taiwan.

Methods

This cross-sectional survey was conducted at oncology outpatient clinics at a medical center in southern Taiwan from June 2011 to Mar 2012. Outpatients who were diagnosed as CML and received imatinib therapy at the clinics were invited to participate the study. The interview survey was consisted of measuring QoL and a semi-structure interview.

Participants' health status at interviews were surveyed by a validated traditional Chinese version of the EuroQol questionnaire which contains a 3-level (no problem, some problems and with problems/difficulties), 5-dimension (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) descriptive system and a 100-mm visual analogue scale (EQ-VAS; range from 0 to 100, represent the worst and the best health-state).

The EQ-5D assessment was transformed into EQ-5D utility index using Japanese tariff [5,6] as there is currently no tariff established for Taiwanese people. The EQ-5D visual analogue scale (VAS) result was divided by 100 to generate a utility value from 0 to 1. An utility instrumentation method published by Furlong et al. (1990) was adopted to derive the TTO utility [7]. The audio-records of interviews were transcribed verbatim and analyzed by constant comparison until reaching saturation of themes.

Descriptive statistics were used to summarize patient characteristics, the results of EQ-5D survey and utility measure. The themes emerged from interview related to participates' perceptions

about QoL measurements and specific attributes to their decisions on different choices for measuring QoL were also analyzed and reported.

Results

Characteristics of participants

Overall, 42 participants were interviewed, their mean age was 50.0 ± 16.0 years old (range: 20 to 80 years), and 23 (54%) were male. Majority of participants (n=35; 83.3%) were diagnosed at chronic phase of CML and 36 (85.7%) participants have been receiving imatinib for more than 1.5 years at the time of interview. Furthermore, 33 (84.6%) and 20 (54.1%) achieved major molecular response and complete molecular response, respectively. However, 13 (31.0%) participants had experienced progression of CML to accelerated phase and 14 (33.3%) participants experienced Grade II thrombocytopenia, and five (11.9%) participants experienced Grade II leukocytopenia during imatinib treatment.

EQ-5D survey

Majority of the 42 participants who completed EQ-5D index survey choose 'no problem' in each dimension. Ten (23.8%) and seven (16.7%) participants reported 'some problems' in pain/discomfort and anxiety/depression dimensions, respectively. Only few participants reported difficulties in the dimensions of mobility (n=3, 7.1%), self-care (n=1, 2.9%) and usual activities (n=2, 4.8%).

There was a higher proportion of participants reported problems and difficulties in those who diagnosed as chronic phase than those diagnosed as accelerated/blast phase in all EQ-5D dimensions, i.e. mobility (8.6% vs. 0%), self-care (2.9% vs. 0%), usual activities (5.7% vs. 0%), pain/discomfort (28.6% vs. 0%) and anxiety/depression (17.1% vs. 14.3%) (Figure 1), however, this may be due to the fact that there were fewer participants diagnosed as accelerated or blast phase when imatinib treatment initiated.

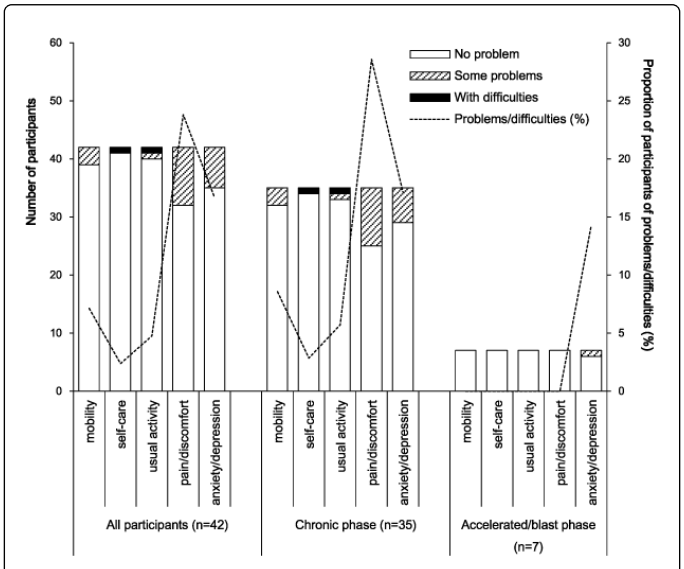

Figure 1: Participants' choices on the five dimensions of EQ-5D index survey

Utility values

The mean utility score derived from EQ-5D index, EQ-VAS and TTO was 0.80 ± 0.08 (range: 0.40, 0.85, mode: 0.85), 0.78 ± 0.13 (range: 0.30, 1.00, mode: 0.8) and 0.80 ± 0.18 (range: 0.13, 0.94, mode: 0.94), respectively. Majority of the participants scored between 0.6 to 1.0 and the proportion were 95.1%, 97.5% and 89.6% for EQ-5D index, EQ-VAS and TTO (Figure 2).

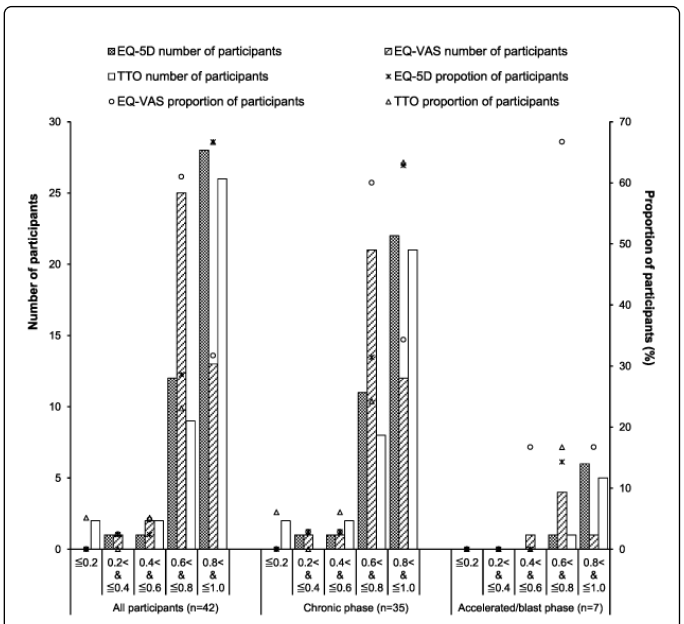

Figure 2: Distribution of the three utility scores in participants with different initial disease phases

Attributes associated with quality of life

Most participants perceived long-term stable control of CML without progression as the treatment target. The interviews emerged that participants had some misconceptions about disease progression and special concerns about imatinib-related side effects, and felt CML limiting their capability of maintaining full functions of a normal life.

Most participants were unclear about the indicators for disease progression and therapeutic target. Recurrent lesions gene (BCR-ABL transcript) tested by polymerase chain reaction was seen as the sign of relapse by some participants even it merely indicates the loss of molecular response to treatment [8].

Although most participants were satisfied with the improvement after imatinib treatment which reflects on participants' EQ-5D index and EQ VAS measures, participants did consider any disease symptom, health-related events or any regular laboratory test results concurrently during the QoL survey. In particular, some participants who indicated 'some problem or with difficult' in "pain/discomfort" dimension mentioned imatinib-related side effects as their main concerns, despite the fact that most side effects such as edema, nausea, vertigo and muscle pain only caused mild discomfort and last for a short period of time; and the most commonly mentioned disease-related symptom was fatigue.

Participants worried interruption and non-adherence of imatinib treatment due to its side effects may lead to potential 'imatinib

resistance'. In fact, in addition to laboratory test results and disease symptoms, imatinib-related side effect was also regarded as an indicator for treatment successes. Participants also worried and regarded persistent bleeding and related potential infections as deterioration of CML.

Most participants were able to maintain daily activities and life functions, such as taking housekeeping duties, sharing family child-care and getting re-employment. However, those who were employed or having future career plans still felt their working capacity was limited and their life were interrupted by regular outpatient visits. Furthermore, the further disability and financial burden caused by disease deterioration was one of participants' main concerns.

Discussion

The three QoL measures are applicable to Taiwanese CML patients, and the mean utility value derived from EQ-5D index and EQ-VAS in the study are similar to normal population in Taiwan [5] and the utility value [3] used in most cost-effectiveness analysis of imatinib for CML patients conducted in different countries. This result may imply that health conditions of CML patients with stable control reflect general population, because the disease symptoms and imatinib-related side effects for most CML patient with long-term imatinib use were relatively mild. In fact, the EQ-5D result of our study cohort is similar to other chronic stable conditions, such as acquired immune deficiency syndrome (range: 0.78-0.95), chronic obstructive pulmonary disease (range: 0.43-0.62) and breast cancer (mean: 0.72), and EQ-5D is the most commonly used QoL measures in cost-effectiveness analysis [9-11].

Alternatively, the result also suggests that EQ-5D index may not capture all the aspects with imatinib treatment or be sensitive to changes in health states. In addition, it seems difficult to make appropriate choices out of the three items in EQ-5D survey. For instance, although participants worried about further treatment effects, most participants chose no problem in the "depression/anxiety" domain as it was difficult to make choice between "some problem" and "with difficult".

In the TTO survey, some participants would accept shorten life years due to their concerns about disease progression, disability and family burden. Therefore, a complementary composite measure provided alongside the QoL measure may broaden the focus beyond health and adopting a wider outlook such as Sen's capability approach, which focuses on what the individual can do not what they do [12].

Although EQ-5D index isn't sensitive enough, EQ-5D, EQ-5D VAS and TTO are applicable to measure utility for CML patients in Taiwan. Although participants receiving imatinib generally presented satisfactory health status, the health status is less known for those who start treatment in accelerated/blast phase, receive other tyrosine kinase inhibitors as first-line therapy, or receive imatinib for more than 18 months. Further studies are still needed to explore underlying attributes about QoL in a wider population, in order to well understand patients' perspective and inform the choice of disease-specific QoL measure.

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