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A Comparison of Five Brief Screening Tools for HIV-Associated Neurocognitive Disorders in the USA and South Africa

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Abstract

Screening for HIV-associated neurocognitive disorders (HAND) is important to improve clinical outcomes. We compared the diagnostic sensitivity and specificity of the mini-mental state examination, International HIV dementia scale (IHDS), Montreal cognitive assessment, Simioni symptom questionnaire and cognitive assessment tool-rapid version (CAT-rapid) to a gold standard neuropsychological battery. Antiretroviral-experienced participants from Cape Town, South Africa, and Baltimore, USA, were recruited. The sensitivity and specificity of the five tools, as well as those of the combined IHDS and CAT-rapid, were established using 2 × 2 contingency tables and ROC analysis. More than a third (65165) had symptomatic HAND. In detecting HIV-D, the CAT-Rapid had good sensitivity (94 %) and weak specificity (52 %) (cut-point ≤10), while the IHDS showed fair sensitivity (68 %) and good specificity (86 %) (cut-point ≤10). The combined IHDS and CAT-rapid showed excellent sensitivity and specificity for HIV-D at a cut-off score of ≤16 (out of 20; 89 and 82 %). No tool was adequate in screening for any HAND. The combination IHDS and CAT-rapid tool appears to be a good screener for HIV-D but is only fairly sensitive and poorly specific in screening for any HAND. Screening for milder forms of HAND continues to be a clinical challenge.

Keywords

HIV-dementia; HIV-associated neurocognitive disorders; Screening

Introduction

HIV-associated neurocognitive disorders (HAND) remain highly prevalent in clinic settings, despite the use of combination anti-retroviral therapy (CART) [1–4]. It is now established

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that HIV-dementia (HIV-D) is diminishing in incidence, but perhaps not prevalence [5, 6]. The less severe form of symptomatic HAND (mild neurocognitive disorder, or MND) and the asymptomatic form (asymptomatic neurocognitive impairment, or ANI) are estimated to occur at rates of 12 and 33 %, respectively, in CART-experienced individuals [4, 7].

These different degrees of HAND are separately diagnosed by the extent of neuropsychological impairment, as well as the presence or absence of functional impairment [8]. HIV-dementia (a “major neurocognitive disorder”) requires there to be impairment in at least two domains of neurocognitive function that are at least 2 standard deviations below normal performance; while for MND and ANI, impairment is of the order of at least one standard deviation worse than normal. When functional impairment is present to a marked degree, together with severe neurocognitive impairment, then HIV-D is diagnosed; when functional impairment is only mild, together with less severe neurocognitive impairment then MND is diagnosed; and when there is no overt functional impairment but mild neurocognitive impairment, then ANI is diagnosed. The diagnosis of a HAND is also one of exclusion. There are several important confounding conditions that may cause or contribute to neurocognitive impairment. These include hepatitis C co-infection, alcohol and substance abuse, and depression [9–11]. Any accurate assessment of HAND must probe for these factors. As common co-morbidities, the extent to which they cause impairment needs to be weighed up.

HIV-D is associated with high rates of mortality, poor medication adherence, and impairment in activities of daily living [12–14]. The effects of MND are, by definition, milder, but those of ANI have been debated [15, 16]. However, there is evidence that ANI may be associated with an increased risk for the development of HIV-D. In such cases, there is an option to intervene by offering CART (in untreated individuals) or neuro-targeted regimens (in those on existing treatment). This may alter the natural history of disease progression in HAND, although there are few longitudinal studies [5, 17, 18]. While there remains some debate on the actual benefit of diagnosing ANI, the argument for neuro-protection might outweigh the risks. In the absence of overt clinical symptomatology, active screening is required to detect cases.

While the gold standard for assessment of HAND is a detailed battery of neuropsychological tests, ideally tapping cognitive domains affected by HIV, these are seldom available to patients in busy settings [8, 19]. Hence, a number of screening tools for HIV-D have been developed and validated for use in these settings. These tools include the HIV dementia scale and the international HIV dementia scale [7, 20, 21]. Other screeners, such as the Montreal cognitive assessment (MOCA) and mini-mental state examination (MMSE) have been used in HIV settings, with varying results [17, 20, 22]. Any screener needs to be brief, easy to administer (by clinicians not trained in neuropsychological assessment), and ought to display adequate sensitivity and specificity.

Most screeners have been developed with HIV-D in mind. In the CART era, and with the growing acceptance that both MND and ANI are important to detect, there is more interest in screening for these milder forms of HAND. The MOCA has been used to detect mild cognitive impairment in geriatric populations, and shows variable sensitivity and specificity

for mild HAND, depending on the cut-off score [23–25]. Similarly, the ability of the IHDS to detect MND and ANI is variable. In one study using a cut-off score of ≤11 to detect HIV-D plus MND, a sensitivity and specificity of 81 and 54 % respectively were reported [12, 26]. Others have reported lower sensitivity to mild HAND [1, 3, 27].

The use of CART may be associated with a change in the type of neuropsychological impairment [5]. Untreated neuro-HIV is thought to be a mainly sub-cortical disease, while treated disease alters this somewhat. Therefore, in populations where CART use is widespread, screeners should tap both cortical and sub-cortical impairment. In addition, the ability to detect milder forms of HAND and to distinguish between them involves high sensitivity not only to neuropsychological impairment, but also to the presence of functional impairment. In this study, we compare the use of five brief screening tools across two sites (one where HIV-B is prevalent, and the other where HIV-C is prevalent). Furthermore, we included a novel screener, the Cognitive Assessment Tool-rapid version (CAT-rapid) to establish its validity in these settings. Our intention was to compare the tools with respect to their ability to screen for HIV-D and for milder forms of HAND.

Methods

Participants

We recruited individuals established on ART in Cape Town, South Africa, and Baltimore, USA. These were participants previously recruited into larger parent cohort studies. In Cape Town, we invited participants who had completed research procedures on a cross-sectional neuro-cognitive and neuro-imaging study, and who had been established on ART for at least 6 months. The Human Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town approved the study. In Baltimore, HIV + individuals who were in a clinical research cohort developed specifically for HAND characterization (the clinical cohort of the NIMH Center for the therapeutics of HAND) were recruited. Sites from South Africa and the USA were selected and the data combined in order to demonstrate that a standard approach to diagnosis and screening might be applicable. A screener used in the USA should also be useful in Africa, India or South America. In addition to the procedures being the same, as well as cross continent case conferences (see below), most of the measures used have been previously reported across various settings.

Assessment and Instruments

The neuropsychological assessment battery was identical across the two sites, and included tests sensitive to the impact of HIV on cognitive function: Tests were grouped into domains of *attention/concentration* [Mental alternation test (MAT), WAIS digit symbol-coding subtest and digit span], *learning/memory* [Hopkins verbal learning test (HVLT) and Rey complex figure test (RCF)], *psychomotor speed* (Grooved pegboard test-dominant and non-dominant) and *executive function* (Color trails test, Stroop color-word test, and the Wisconsin card sorting test (WCST). For each test, a raw score was obtained, together with a standard deviation, based on control or normative data available for the site. We assigned a neuropsychological score of 2 (NP2) if the performance was poorer than 2 standard deviations (SD) from the mean on at least two domains; or more than 2 SD's on one domain

and at least 1 SD on two other domains. We assigned an NP score of 1, if the performance was poorer than 1 SD on at least 2 domains.

The five screening tools compared in this study were the:

- **i.** International HIV dementia scale (IHDS) [7]. The IHDS has been validated in numerous settings, including the USA and South Africa [12]. It has established sensitivity for detecting HIV-dementia, and may be useful for milder forms of HAND [15]. The IHDS includes measures of psychomotor speed and processing, as well as short-term memory.
- **ii.** The Montreal cognitive assessment (MOCA). The MOCA has been used in HIV-infected individuals [17]. It does not measure psychomotor speed or processing, but includes measures of executive function, attention, language, and episodic memory.
- **iii.** The mini-mental state examination (MMSE). The MMSE has been extensively used and studied since its original description [19]. Its limitations in HAND detection have been noted [20].
- **iv.** The Simioni symptom questions (SSQ). These questions were derived from the approach described by Simioni et al., and which proved to be useful in a first-tier screening approach. Patients without complaints were not found to have HIV-dementia, although they might have milder HAND [22].
- **v.** The cognitive assessment tool-rapid version (CAT-rapid). The CAT-rapid was developed by the first author (JJ), in response to the need to develop a brief HAND screening tool that includes functional symptom questions and a measure of executive function (see Appendix 1). The CAT-rapid includes four symptom questions, registration of four words, a mini-trail-making test of four letter/number pairs, and word recall.

In addition to these tools, we also used the combined performance of the IHDS (scored out of a possible 12 points) and the CAT-rapid (scored out of a 8 points discarding the 4-word recall), to arrive at a combined tool total score of 20. This “6th tool” was also included in the analysis.

We administered the centres for epidemiological studies-depression (CES-D) scale and the substance abuse and mental illness screener (SAMISS) to confirm the presence or absence of significant depressive symptomatology or alcohol abuse. Both have been extensively used and validated in international settings (see [23, 28]).

Functional impairment was ascertained in three ways: firstly, establishing self-reported ART adherence of >80 %; secondaly by administration of the modified Lawton Activities of daily living scale (LADL) [26]; and thirdly the presence of a positive response to functional symptoms reported on the SSQ and CAT-rapid. We assigned a functional assessment (FA) score of two (marked impairment), if the participant scored 14 or less on the LADL, OR 15 AND was noted to have an adherence problem. We scored FA1 if the LADL score was 15

OR there was either an adherence problem or a self-reported functional problem on the SSQ or CAT-rapid.

Procedures

Participants were administered the five screening tests, a detailed neuropsychological test battery, an assessment of activities of daily living and of subjective adherence, and a neuro-medical assessment. Participants in Cape Town did not have hepatitis C testing (as the population prevalence is approximately 6 %), while those in Baltimore did [29]. Cases were classified into HAND categories using American Academy of Neurology criteria. HAND diagnosis was confirmed by regular case conferences of all individuals from both sites by the PIs (JJ and NS) at each site. The order of testing was the same across both sites: We administered the IHDS, SSQ, CES-D, AUDIT and CAT-rapid, followed by the detailed battery. After the battery, we completed the assessment by administering the MMSE, functional assessment measures, and MOCA. The full battery including screeners took approximately 2 h and 30 min. The administration times of the screeners were: IHDS took 4 min, the SSQ took 3 min, the CAT-rapid took 7 min, the MOCA took 13 min, and the MMSE took 12 min.

Analysis

For each screener and AAN HAND category, participants were coded as “0” for normal and “1” for neurocognitive impairment. We used three groups of impairment as follows to establish sensitivity and specificity of each tool for various levels and types of impairment: [1] All three forms of HAND, [2] Symptomatic HAND: MND and HIV-D, and [3] HIV-Dementia. According to the established cut-off points for each tool, participants scoring above the cut-off point were coded as “0” (cognitively intact according to the screener), and those at or below the cut-off point were coded as “1” (cognitively impaired). We then generated a series of 2 × 2 contingency tables for the screeners versus the AAN HAND classification. The output displayed the number of true positives, true negatives, false positives and false negatives of the CAT-Rapid at the specified cut-off point. We then determined the tool’s sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) at the specified cut-off point using http://www.medcalc.org/calc/diagnostic_test.php. The value of the PPV is that it is a measure of how many cases are detected by the tool, including those incorrectly included as cases, and therefore requiring further investigation to confirm; the PPV is of greater use where the proportion of “diseased” individuals in the study is similar to the general prevalence. The NPV is a measure of the proportion of cases that are discarded as non-cases, including those that were in fact cases, but missed. In principle for screening, high NPV’s are regarded as important. We report on sensitivity and specificity for each screener’s ability to detect HIV-D and any form of HAND. We regarded a value of >80 % as good sensitivity and >80 % as good specificity to maximize the utility of the respective screening tool.

Results

The sample included 156 participants (89 from SA, 67 from the USA). The sample median age was 40 years, and median education was 11 years. Nearly two-thirds (62.80 %) of the

sample was female, and the median CD4 cell count was 460 cells/ml (see Table 1). Regarding confounders, we noted that in Baltimore, the average CES-D score was 10,13 (SD = 10.54); while in Cape Town it was 7,00 (SD = 9,90). Hazardous alcohol use in the preceding 3 months was reported in 5 participants in Baltimore and 4 in Cape Town. While hepatitis C infection status was not investigated in Cape Town, the prevalence in the Baltimore sub-sample was 38.8 %.

Nearly half of the participants had symptomatic HAND: 46 (29 %) were classified as mild neurocognitive disorder (MND) and 19 (12 %) as having dementia (HIV-D)]. There were more participants with HIV-D in the USA (15, or 22 %) versus South Africa (4, or 5 %). There were significant differences between the HAND categories with respect to gender (there were more men with HIV-D); age (people with HIV-D were older); and CD4 cell count (participants with HIV-D had higher CD4 cell counts at the time of the assessment). There were no between-category differences with respect to level of education.

Table 2 presents the screening properties of the 5 tools.

Screening for HIV-D

The CAT-Rapid had good sensitivity and fair specificity while the IHDS showed fair sensitivity and good specificity. The MOCA showed excellent sensitivity but poor specificity.

Screening for Any HAND

No tool met the above criteria. The IHDS displayed poor sensitivity and good specificity, the MOCA again showed high sensitivity but weak specificity, while the SSQ and CAT-rapid showed fair sensitivities and fair-to-poor specificity.

Screening for Symptomatic HAND

While no tool met the criteria of good sensitivity and fair specificity, the CAT-rapid had good sensitivity and fair specificity, while the IHDS showed fair sensitivity and good specificity The MOCA and SSQ showed good to fair sensitivity, but poor specificity.

Table 3 presents the performance of the combined IHDS and CAT-rapid at several possible cut-off scores for HIV-D and any HAND. The combined tool showed excellent sensitivity and specificity for HIV-D at a cut-off score of ≤16 (89 and 82 %), while a score of ≤17 yielded results nearly as good (89 and 64 %). The ROC curve is presented in Fig. 1, with AUC of 0.89. The optimal cut-off for detecting any HAND may be regarded as either ≤17 or ≤18. Figure 2 presents the ROC curve supporting this interpretation. The IHDS/CAT-rapid combined tool performed the best out of all the screeners for HIV-D. In screening for any HAND, it was an improvement over the other screeners, but was still not optimal.

Discussion

Few studies have compared several brief screening tools against a gold standard neuropsychological test battery in CART-experienced participants. We have demonstrated that both the IHDS and CAT-rapid are useful in screening for HIV-D. We confirm, as others

have, that the MMSE has relatively poor sensitivity [20, 30]. No single tool proved to be ideal in screening for symptomatic HAND, although the CAT-rapid displayed fair sensitivity (78 %) with only weak specificity (54 %), while the IHDS showed weak sensitivity (52 %) and good specificity (86 %). The combined IHDS and CAT-rapid tool displayed improved sensitivity (89 %) and specificity (82 %) over all the other tools for HIV-D, but could not improve on the CAT-rapid or IHDS for any HAND screening.

The issue of screening for HAND has received support from some but not all groups [31, 32]. There seems to be little debate regarding screening for symptomatic forms of HAND (HIV-D and MND) [33]. Searching for ANI cases runs several risks, including the potential for over-diagnosis, distress to asymptomatic individuals receiving a diagnosis, uncertainty regarding treatment, and resources required for detecting these disorders [16]. In sub-Saharan Africa and other resource-limited settings (RLS), this is of critical concern, particularly as access to detailed neuropsychological testing is very limited. In addition, the ability of busy clinic staff to assess, treat and remove potential confounding conditions is also limited. We propose that screening for HIV-D be regarded as a priority. We confirm that the IHDS and the new tool (CAT-rapid) perform adequately for this purpose. Individuals in RLS who screen positive for HIV-D should receive additional assessment. The extent of this will depend on the clinical presentation and access to facilities. A pragmatic approach might be to (i) confirm the presence of severe neurocognitive impairment using additional screeners or tests (such as combined screeners, or additional tests where technicians are available), (ii) established the extent of functional impairment, (iii) assess for alcohol and substance abuse and depression (using tools such as the substance abuse and mental illness screener, or PHQ-2), and (iv) assess for biological factors depending on context (such as hepatitis C, syphilis or vitamin deficiency) [28, 34]. This type of screening program, if widespread, would require training and support. Some non-medical personnel may struggle in the administration of measures [27]. Another challenge is that patient report of functional impairment is often poor [4, 35].

Many screening tools are limited with respect to detecting mild HAND (either symptomatic or asymptomatic). We confirm this challenge. It may be that the signal from less severe disease is too weak for brief tests to measure. In this study, the MoCA displayed good sensitivity for any or symptomatic HAND, but poor specificity. One group has criticized the MoCA for its inability to provide a true quantitative measurement of cognition [13, 14, 33], while others note that certain items may be culturally insensitive [16, 36]. We have found similar limitations in detecting mild HAND with respect to the IHDS. Even using the cut-point of ≤11 did not improve sensitivity beyond 69 % for detecting any HAND (data not shown). The CAT-rapid at a cut off of ≤10 showed some utility for detecting symptomatic HAND but not any HAND, most probably due to the inclusion of the 4-symptom questions. In this study, the SSQ showed fair sensitivities across the range, but poor specificity, most likely reflecting the need for an objective measurement of cognition.

Screening tools by definition tap only some neurocognitive domains, and then only using one short test. It is possible that differences between individuals, as well as stages of infection may affect test performance. For example, differences in neuropsychological performance in CART-naïve versus experienced individuals may exist. Several authors have

noted that, in untreated disease, sub-cortical features (such as psychomotor slowing and impaired retrieval of previously-learned information) are prominent, while in CART-experienced individuals, learning and executive functions may be impaired [5, 18, 37]. Therefore tools that tap psychomotor function (such as the IHDS) might be less useful for CART-experienced individuals, and more so when those features are mild.

In addition to potential differences between regions with respect to biologic factors, the issue of cultural and language differences may hinder screening and diagnostic efforts. Many of the screeners have been validated in low-resourced settings (for example the IHDS) (see [12, 38, 39]). Others have been researched but present issues of cultural fairness, for example the MOCA (see [40]). The use of control data may in part mitigate these effects, but further work to ensure that over-diagnosis does not occur should be done.

The combined IHDS/Cat-rapid displayed promise as a screener for HIV-D and was the best performer of all the tools in this regard. This may be a result of the effect of including measures of psychomotor functioning, memory, and executive function. The tool, however, was only marginally useful in detecting, at a cut-off of ≤18, any HAND. It had low sensitivity at this point.

So while the value of screening for mild and asymptomatic HAND is debated, an ideal approach to screening for them remains elusive. While tools such as the MoCA and combined IHDS/CAT-rapid display good-to-fair sensitivity, they display poor specificity. Using such tools is therefore likely to result in a number of false-positive tests and patients without any HAND referred for fuller neuropsychological assessment. An “intermediate level of assessment may improve these outcomes. This might entail an ultra-short battery of tests, or expanded set of screeners. While the screeners used in this study typically take 4–10 min to complete, an “intermediate” assessment test may take 10–30 min to complete (see for example [41]). In resource-limited settings, the absence of experienced technicians and neuropsychologists, these professionals may compound the problem. Improving the tools may improve the capacity, and mobile health tools using brief batteries are beginning to come to the fore [42].

This study was limited by the fact that there were some between-site differences-such as in the prevalence of HIV-D. Assumptions were made regarding the respective HAND prevalence across regions whether HIV-B and HIV-C respectively are prevalent. To some extent, it is now being accepted that rates of HAND in these settings are similar [43, 44]. In addition, at neither site did we have detailed objective measures of functional impairment. Instead, we relied on self-report and neurologic examination findings. We note also that the majority of the sample was female-approximately two-thirds. We confirm here, as in previous studies, that male gender confers a greater risk of HIV-D. In South Africa, the epidemic affects mainly women. While the reasons for male preponderance of impairment are unclear, it may reflect biological issues (such as higher rates of alcohol and substance abuse co-morbidity) and/or psychosocial issues (such a lower rates of health-seeking and therefore greater immuno-compromise).

While detecting HIV-D using screeners appears to be a tractable problem, albeit requiring training and supervision of staff, screening for milder forms of HAND continues to be a clinical challenge. An improved screener for these forms of HAND may require the inclusion of additional tests to enhance both sensitivity and specificity. Future studies may include sub-analysis of detailed neuropsychological batteries of impaired individuals to identify additional tests that tap mild to moderate impairment and that can be modified into brief and ecologically valid versions.

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Appendix 1: Cognitive Assessment Tool-Rapid Version (CAT-Rapid)1

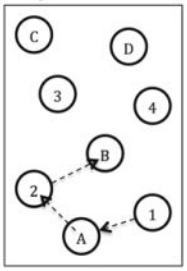
Cognitive Assessment Tool- Rapid Version (CAT-Rapid)[1]

1. Symptoms- *Ask the patient the following questions exactly as they are written:*
"Compared to your best:
- do you often have problems remembering information? Y=0 N=1
- are your hands clumsy, shaky or weak? Y=0 N=1
- have you found it hard to follow a conversation or a story? Y=0 N=1
- do you have trouble planning or doing daily activities? Y=0 N=1 _ / 4

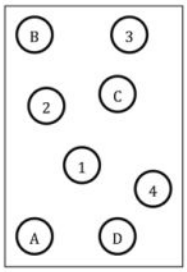
Word Registration- *Give 4 words to recall (apple, watch, table, red), reading one second for each. Ask the patient to repeat them. If not correct say words again. Tell patient you will ask for all 4 words a bit later.*

2. Trail-making: *Ask the patient to draw a line connecting the numbers and letters starting from the lowest number. They must switch between the letters and the numbers from start to finish. The example shows how to do it. They should go as quickly as they can without making mistakes.*

Example



Test



Score 1 point for each correct pair of number/letter: _ / 4

3. Word recall: Ask the patient to recall the 4 words. For words not recalled, provide a clue (for apple- "fruit", for watch- "jewelry", for table- "furniture", for red- "colour"). Score 1 point for spontaneous recall of a word and ½ for prompted recall. _ / 4

Total CAT-Rapid score: Add scores for 1. – 3. together to a maximum of 12 points. _ / 12

Interpretation:
>10: this score suggests that a diagnosis of dementia is unlikely. Consider another cause for symptoms or refer for further opinion or testing.
Score <10: this score suggests that dementia may be present. Confirm the diagnosis by excluding contributory causes, applying clinical judgement and performing investigations as indicated. Consider referring for further opinion or testing.

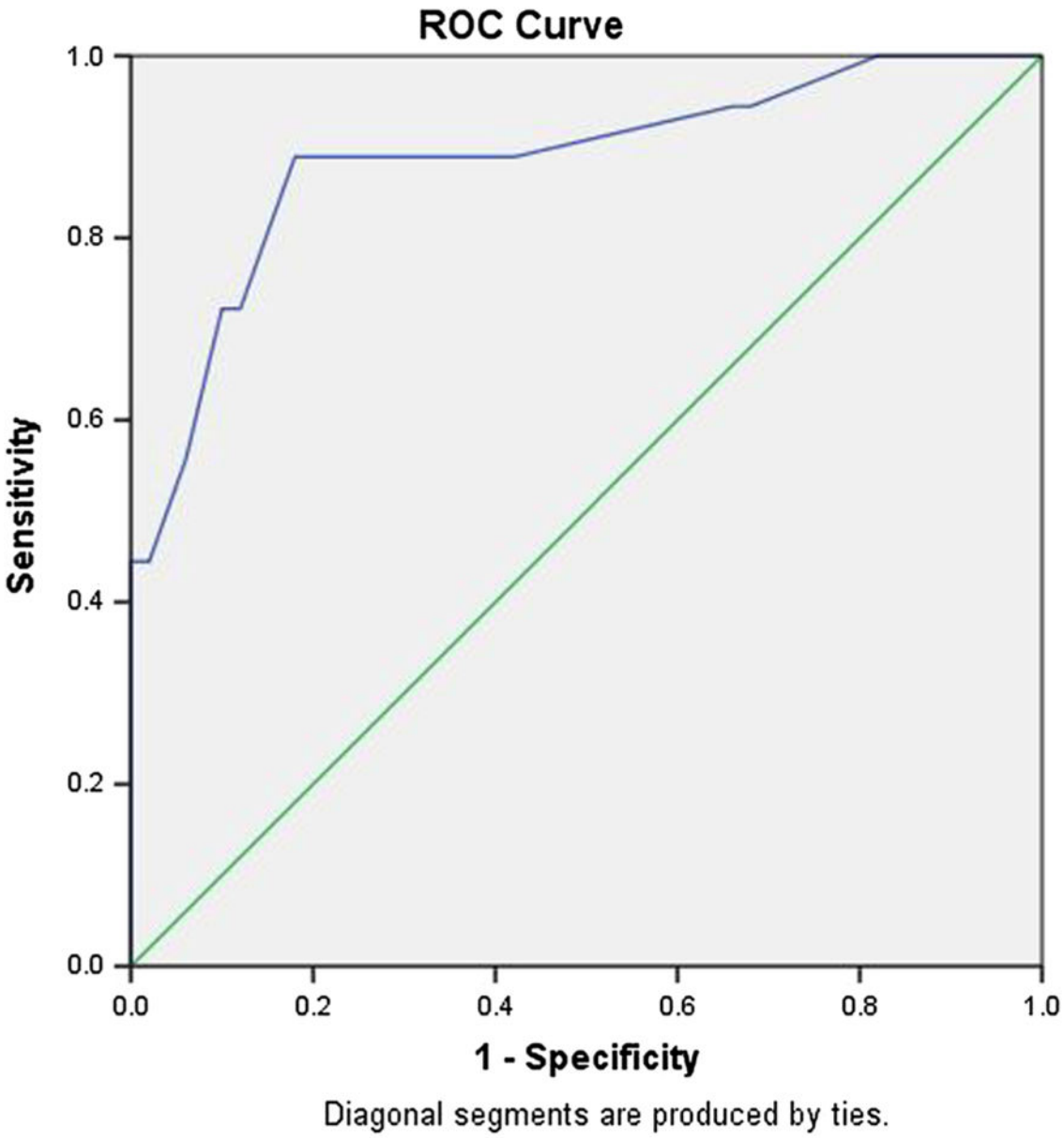


Fig. 1.

Receiver operating characteristic curve, Combined IHDS and CAT-Rapid. Normal versus HIV-Dementia. Area under the curve = .886

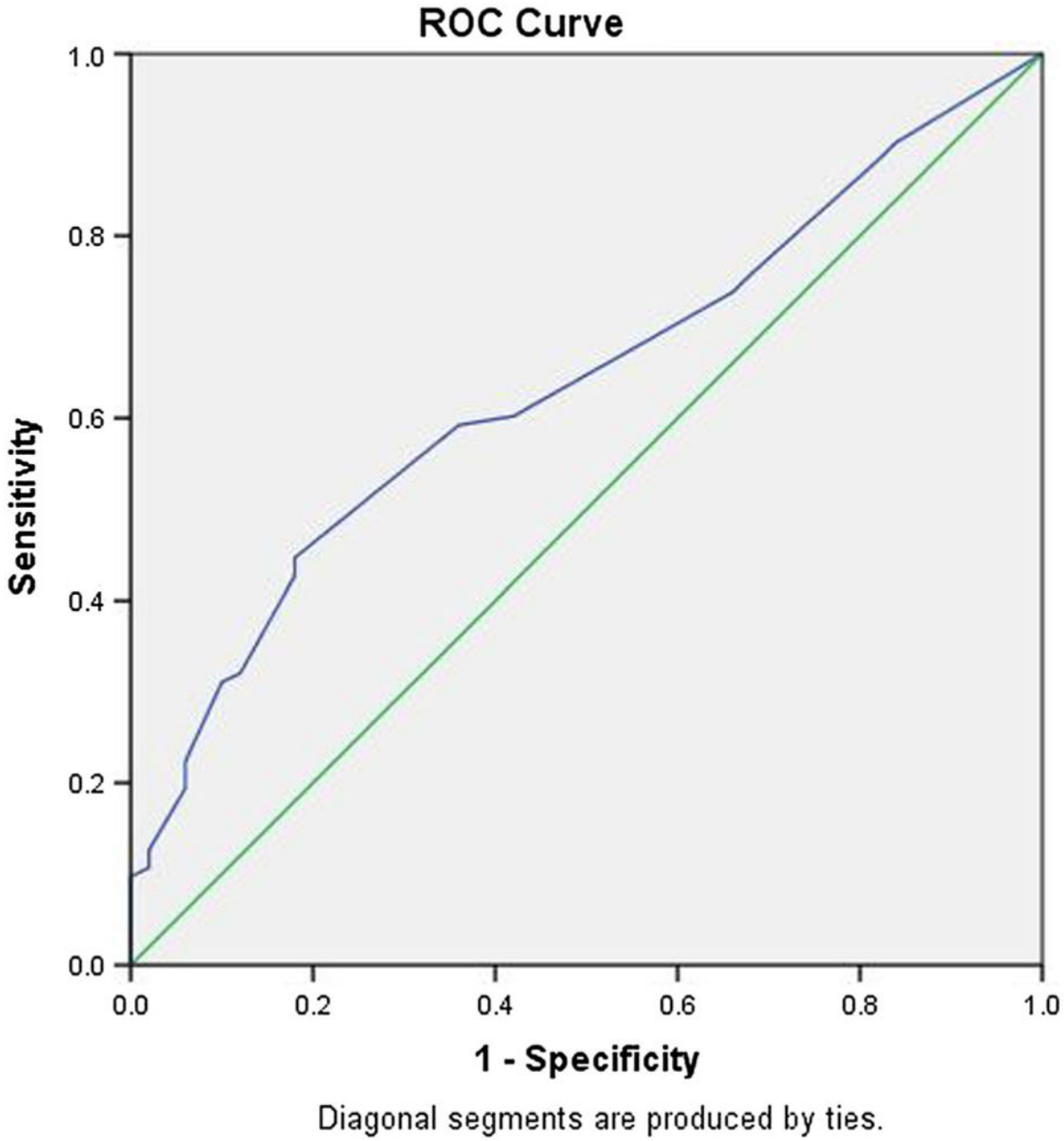


Fig. 2.

Receiver operating characteristic curve, Combined IHDS and CAT-Rapid. Normal versus HAND. Area under the curve = .638

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Table 1

Characteristics of participants by HAND category

Characteristics	N	Normal	ANI	MND	HIV-D	*p* value
Total	156	50	41	46	19	
SA	89	39	24	22	4	
USA	67	11	17	24	15	
Female, No. (%)	98	36 (72.0)	31 (75.6)	25 (54.3)	6 (31.4)	.003
Black race (%)	0	43(87.8)	37(90.2)	39 (84.8)	14 (77.8)	.586
Age, No. (years)	154	49	40	46	19	.001
Median		35.0	38.5	44.5	54.0	
Interquartile range		13.5	24.3	26.5	16.0	
Education, No. (years)	154	50	39	46	19	.289
Median		11.0	11.0	11.0	12.0	
Interquartile range		1.3	2.0	2.0	3.0	
Hazardous drinking, No. (%)	0	2 (4.2)	3 (7.7)	3 (6.8)	1 (5.6)	.923
CES-D score	154	49	41	46	18	.000
Median		5	4	7	28	
Interquartile range		11.0	11.0	16.0	31.5	
Viral load suppressed, No. (%)	95	25 (89.3)	19 (86.4 %)	28 (96.6 %)	14 (93.3 %)	.839
CD4 Nadir/baseline, No, cells/ml	144	46	38	44	16	.691
Median		178.5	268.5	197	140.5	
Interquartile range		84.5	74.25	76.0	60.5	
CD4 count, No., cells/ml	124	43	33	32	16	.006
Median		363.0	498.0	454.0	635.5	
Interquartile range		300.0	229.0	329.5	460.8	

SA South Africa, *USA* United States of America, *ANI* asymptomatic neurocognitive impairment, *MND* mild neurocognitive disorder, *HIV-D* HIV-dementia

Table 2

Sensitivity and specificity of the five screening tools for HIV-D, any HAND and symptomatic HAND

Cut-off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
IHDS (≤10)				
Normal vs. HAND	40.95	86.00	86.00	40.95
Normal vs. Symptomatic	51.56	86.00	82.50	58.11
Normal vs. HIV-D	68.42	86.00	65.00	87.76
IHDS (≤11)				
Normal vs. HAND	64.76	62.00	78.16	45.59
Normal vs. Symptomatic	68.75	62.00	69.84	60.78
Normal vs. HIV-D	73.68	62.00	42.42	86.11
MoCA (≤26)				
Normal vs. HAND	89.32	22.45	70.77	50.00
Normal vs. Symptomatic	90.48	22.45	60.00	64.71
Normal vs. HIV-D	100.00	22.45	32.14	100.00
MMSE (≤24)				
Normal vs. HAND	23.81	97.96	96.15	37.50
Normal vs. Symptomatic	24.62	97.96	94.12	49.48
Normal vs. HIV-D	26.32	97.96	83.33	77.42
SSQ (≥1)				
Normal vs. HAND	77.64	32.00	69.37	35.56
Normal vs. Symptomatic	75.38	32.00	59.04	50.00
Normal vs. HIV-D	78.95	32.00	30.61	80.00
CAT-Rapid (≤10)				
Normal vs. HAND	64.42	52.00	73.63	41.27
Normal vs. Symptomatic	78.12	52.00	67.57	65.00
Normal vs. HIV-D	94.44	52.00	41.46	96.30

IHDS International HIV-Dementia Scale, *MoCA* Montreal Cognitive Assessment, *MMSE* Mini-mental state examination, *SSQ* Simioni, Symptom Questionnaire, *CAT-Rapid* Cognitive Assessment Tool-Rapid, *HAND* HIV-associated neurocognitive disorder = Asymptomatic Neurocognitive Impairment or Mild Neurocognitive Disorder or HIV-Dementia, *HIV-D* HIV Dementia, *PPV* positive predictive value, *NPV* negative predictive value. Combined scores unavailable for 3 participants ($N = 153$)

Table 3

Sensitivity and specificity for cut-off points of the combined CAT-Rapid and IHDS (maximum score obtainable = 20)

Cut-off Point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≤15				
Normal vs. HAND	31.00	90.00	84.49	38.79
Normal vs. HIV-D	72.22	90.00	72.22	90.00
≤16				
Normal vs. HAND	42.72	82.00	83.02	41.00
Normal vs. HIV-D	88.89	82.00	64.00	95.35
≤17				
Normal vs. HAND	59.22	64.00	77.22	43.24
Normal vs. HIV-D	88.89	64.00	47.06	94.12
≤18				
Normal vs. HAND	73.79	34.00	69.72	38.64
Normal vs. HIV-D	94.44	34.00	34.00	94.44
≤19				
Normal vs. HAND	88.35	18.00	68.94	42.86
Normal vs. HIV-D	100.00	18.00	30.51	100.00

CAT-Rapid Cognitive Assessment Tool-Rapid, *IHDS* International HIV-Dementia Scale, *HAND* HIV-associated neurocognitive disorder = Asymptomatic Neurocognitive Impairment or Mild Neurocognitive Disorder or HIV-Dementia, *HIV-D* HIV Dementia, *PPV* positive predictive value, *NPV* negative predictive value. Combined scores unavailable for 3 participants ($N = 153$)