



# One center's experience with complications during the Wada test

\*Nicholas J. Beimer, ††Henry A. Buchtel, and \*Simon M. Glynn

*Epilepsia*, 56(8):e110–e113, 2015  
doi: 10.1111/epi.13046

## SUMMARY

This study aimed to define the number and type of complications associated with the Wada test at an academic medical center for comparison to previous reports. We performed a retrospective review of medical records for patients who underwent the Wada test at the University of Michigan between April 1991 and June 2013. Information was collected regarding the angiography procedure and the immediate postoperative period to assess for both clinical and angiographic complications. A total of 436 patients were identified who underwent the Wada procedure between April 1991 and June 2013, and 431 patients were included in the final analysis. Twenty-five patients (5.8%) had notable clinical events associated with the Wada test. Nine patients (2.1%) had clinical events meeting criteria for complication, which included seizures, status epilepticus, internal carotid artery vasospasm, inadvertent injection of anesthetic in the external carotid artery, and transient encephalopathy. No complications were associated with significant morbidity or mortality. This retrospective review of patients undergoing the Wada test found significantly fewer associated complications in comparison to previously published studies, with no patients experiencing long-term morbidity. The Wada test should be considered a safe diagnostic tool for lateralizing language and memory.

**KEY WORDS:** Wada test, Complications, Intracarotid amobarbital procedure.



**Dr. Nicholas J. Beimer** is a clinical neurophysiology fellow at the University of Michigan.

The Wada test, or intracarotid amobarbital procedure (IAP), is often used to determine language and memory lateralization in candidates for epilepsy surgery, and has been referred to as the “gold standard” for this purpose. However, with the development of noninvasive functional neuroimaging methods, including functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and transcranial magnetic stimulation (TMS) to lateralize language function, the continued use of the Wada test has been questioned.<sup>1–3</sup> One reason is that the Wada test is invasive, as it requires the insertion of a catheter into the internal carotid artery (ICA). The complication rates associated with cerebral angiography and Wada testing range from 0.3% up

to nearly 11% of patients undergoing the procedure, with the Wada test reported near the upper end of this range.<sup>4–7</sup> With this knowledge, it makes sense to question the continued use of a decades old invasive test as the primary modality for lateralizing language and memory. However, in contrast to previous reports citing complications in nearly 11% of patients, our experience has been that the Wada test is a relatively safe procedure. We report our experience at an academic medical center for comparison to previous reports, to accurately define the risks associated with the Wada test.

## METHODS

Institutional review board approval was granted prior to beginning the study (study ID# HUM00057420). A database of patients who underwent the Wada test between April 1991 and June 2013 at the University of Michigan was used to perform a retrospective chart review. Data were collected on the occurrence of any significant clinical event (e.g., seizures, groin hematomas, unanticipated change in neurologic

Accepted April 30, 2015; Early View publication June 4, 2015.

Departments of \*Neurology and †Psychiatry, University of Michigan, Ann Arbor, Michigan, U.S.A.; and ‡Neuropsychology Section, VA Ann Arbor, Ann Arbor, Michigan, U.S.A.

Address correspondence to Nicholas J. Beimer, Department of Neurology, University of Michigan, 1500 E. Medical Center Dr., Ann Arbor, MI 48109, U.S.A. E-mail: nbeimer@med.umich.edu

Wiley Periodicals, Inc.

© 2015 International League Against Epilepsy

condition, and failure to complete testing due to an unexpected clinical event) that occurred at the time of Wada testing, during the peri-angiography period, or within 1 month of the procedure. A procedure complication was defined as an unintended adverse and undesirable development in a patient that was clinically significant, requiring medical treatment, additional resource use, or prolonged hospitalization. Any unanticipated change in neurologic condition during or immediately after the procedure was deemed to be procedure related. Neurologic changes related to the patient's underlying illness (e.g., seizures in patients with known intractable epilepsy) were not considered procedure-related complications. Arteriotomy-related hematomas were considered complications if they required consultative evaluation, treatment, or prolonged hospitalization. Patients undergoing procedures immediately following Wada testing (e.g., embolization) were excluded due to an inability to distinguish complications associated with the procedure from complications associated with the Wada test. Calculation of percent complications was performed using Microsoft Excel.

All Wada tests were performed by first gaining arterial access with micropuncture and Seldinger technique, using either 5- or 4-French sheaths. Catheterization of the ICA was then performed and a road map was created by conventional angiography. Anesthetic was then given by hand-push injection. Amobarbital was used exclusively as the anesthetic of choice until May 1998, at which point either methohexital or amobarbital was used. Amobarbital was no longer used after July 2004, with methohexital being used exclusively through June 2013. Dosing used for amobarbital was typically a single injection of 100–125 mg into each ICA. Dosing used for methohexital was typically 5–7 mg into each internal carotid artery, divided into two doses. Additional procedure details can be found in previously published reports on the use of amobarbital and methohexital for the Wada test.<sup>8,9</sup>

## RESULTS

Of 436 patients who underwent the Wada test between April 1991 and June 2013 at the University of Michigan, a total of 431 patients were included for review. Four patients were excluded due to lack of documentation in the electronic medical record, and one patient was excluded because he had an embolization procedure for an arteriovenous malformation immediately following the Wada test. Of 431 patients, a total of 25 (5.8%) experienced an unintended clinical event during or immediately after the Wada test, although only 9 (2.1%) of those patients had clinical events meeting our criteria that were considered complications. A summary of all unintended clinical events, as well as those events meeting criteria to be considered complications, can be found in Table 1, with details of each of the complications found in Table 2.

**Table 1. Procedure-related clinical events and complications during Wada testing among 431 reviewed cases**

Clinical event	Number of patients (%)	Number of patients meeting criteria for complication (%)
Arteriotomy-related hematoma	13 (3.0)	0 (0)
Encephalopathy	3 (0.7)	3 (0.7)
Injection of external carotid artery	1 (0.2)	1 (0.2)
Internal carotid artery vasospasm	2 (0.5)	2 (0.5)
Seizure	6 (1.4)	2 (0.5)
Status epilepticus	1 (0.2)	1 (0.2)
Total	25 (5.8) <sup>a</sup>	9 (2.1)

<sup>a</sup>One patient had both an arteriotomy-related hematoma and a seizure.

Among the patients who had arteriotomy-related hematomas, none met criteria considered to be complications, as none required additional resource use or deviation from the usual postoperative observation and care. Of the six patients who had seizures around the time of the Wada test, two were considered to be complications, as they occurred during the procedure and resulted in repeating Wada testing at a later date due to the patients being in a postictal state. Of note, one patient had a seizure prior to injection of anesthetic but after angiography, which suggests that the seizure was coincident with the test, as opposed to causally related. All three patients with encephalopathy had transient alteration of consciousness after the first injection of anesthetic, which precluded completion of Wada testing, requiring repeated testing at a later date. One patient had right ICA vasospasm with luminal filling defects and reported numbness and tingling in the left finger tips during the procedure, which resolved by completion of the procedure. This event was concerning for a transient ischemic attack (TIA). This patient had the Wada test completed at a later date. A second patient had ICA vasospasm on the left side, followed by complete resolution of vasospasm after verapamil infusion during the same procedure. This event was considered a complication due to requirement for medical treatment. One patient had anesthetic inadvertently injected into the external carotid artery twice during the same test, with conflicting neuropsychological testing results after eventual successful injection of both ICAs, prompting repeated Wada testing at a later date due to concern for an encephalopathy confounding the results. Finally, one patient was hospitalized for 2 days for status epilepticus, with the presumed cause due to delayed administration of the patient's scheduled antiepileptic doses during the day of Wada testing. No long-term morbidity was associated with this complication.

## DISCUSSION

The percentage of patients who had a complication during the Wada test between April 1991 and June 2013

**Table 2. Clinical details of nine patients who experienced unintended clinical events, which met criteria to be considered complications**

Complication	Clinical details	Criteria met to be considered complication	Date of Wada test	Age (years)	Gender	Anesthetic
Encephalopathy	Wada repeated due to inability to perform testing during second injection	Additional resource use	November 12, 1991	41	Female	Amobarbital
Encephalopathy	Wada repeated due to inability to perform testing during second injection	Additional resource use	November 17, 1993	37	Male	Amobarbital
Encephalopathy	Wada repeated due to inability to perform testing during second injection	Additional resource use	February 1, 1999	44	Female	Amobarbital
Anesthetic injection into ECA	Inconsistent responses during Wada test, possible encephalopathy Wada later repeated to validate results	Additional resource use	December 7, 1992	23	Female	Amobarbital
Seizure	Seizure after angiography was completed, before anesthetic injection Wada later repeated due to postictal state	Additional resource use	July 9, 1991	10	Male	Amobarbital
Seizure	Seizure after first anesthetic injection Wada later completed due to postictal state	Clinically significant neurologic change and additional resource use	November 17, 1992	34	Male	Amobarbital
Status epilepticus	Missed medication dose during day of testing resulting in status epilepticus and 2-day hospitalization for treatment and observation	Clinically significant neurologic change and additional resource use	May 3, 2010	9	Male	Methohexital
ICA vasospasm	Resolved following infusion of verapamil No transient or permanent neurologic changes	Medical treatment	March 21, 2007	21	Female	Methohexital
ICA vasospasm	TIA (clinically significant neurologic change, with subsequent resolution) Wada later completed after resolution of vasospasm	Clinically significant neurologic change, medical treatment, and additional resource use	May 17, 2006	46	Male	Methohexital

ECA, external carotid artery; ICA, internal carotid artery; TIA, transient ischemic attack.

at the University of Michigan was 2.1%. One pooled multicenter, combined study of patients who underwent Wada testing between 2000 and 2005 reported that 1.09% of patients had a complication,<sup>4</sup> which is similar to our result, as well as that reported for general cerebral angiography (0.3–1.3%).<sup>5,6</sup> In contrast, a single-center study from 2008 by Loddenkemper et al. reported complications in up to 10.9% of cases, which is cited frequently in recent literature discussing the relative safety of the Wada test for language lateralization.<sup>7,10</sup> These discordant data may reflect a distinction between reporting unintended, insignificant clinical events associated with the Wada test versus significant complications.

Understanding these risks is important, as the Wada test clearly remains useful in patients without clear language lateralization or with suspected atypical language lateralization.<sup>10</sup> When contemplating the risks and benefits of performing the Wada test, an additional factor to consider is the variability among medical centers and clinicians with regard to experience and expertise, and the impact this may have on complication rates. Despite recent advances, a similar argument should also be made for noninvasive

functional tests, as the ability of functional magnetic resonance imaging (fMRI) to predict postsurgical memory outcomes has yet to be reliable or validated across centers and requires additional investigation.<sup>11,12</sup> Although the reliability of the Wada test for lateralizing memory has been disputed, it can predict postsurgical memory impairment, and thus remains clinically important in some patients with epilepsy.<sup>13</sup> Therefore, the Wada test should remain an important diagnostic option for patients with epilepsy who are candidates for epilepsy surgery.

## ACKNOWLEDGMENTS

The authors would like to thank the staff and technologists of the Clinical Neurophysiology Laboratory and the Neuroradiology Department at the University of Michigan. The authors would also like to particularly thank Dr. Ravi Shastri for his thoughtful input regarding this study.

## DISCLOSURE

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## REFERENCES

1. Binder JR. Functional MRI is a valid noninvasive alternative to Wada testing. *Epilepsy Behav* 2011;20:214–222.
2. Papanicolaou AC, Rezaie R, Narayana S, et al. Is it time to replace the Wada test and put awake craniotomy to sleep? *Epilepsia* 2014;55:629–632.
3. Mathern GW, Beninsig L, Nehlig A. From the editors: Epilepsia's survey on the necessity of the Wada test and intracranial electrodes for cortical mapping. *Epilepsia* 2014;55:1887–1889.
4. Haag A, Knake S, Hamer HM, et al. The Wada test in Austrian, Dutch, German, and Swiss epilepsy centers from 2000 to 2005: a review of 1421 procedures. *Epilepsy Behav* 2008;13:83–89.
5. Fifi JT, Meyers PM, Lavine SD, et al. Complications of modern diagnostic cerebral angiography in an academic medical center. *J Vasc Interv Radiol* 2009;20:442–447.
6. Willinsky RA, Taylor SM, TerBrugge K, et al. Neurologic complications of cerebral angiography: prospective analysis of 2,899 procedures and review of the literature. *Radiology* 2003;227:522–528.
7. Loddenkemper T, Morris HH, Möddel G. Complications during the Wada test. *Epilepsy Behav* 2008;13:551–553.
8. Milner BM. Psychological aspects of focal epilepsy and its neurosurgical management. In Purpura DP, Penry JK, Walter RD (Eds) *Advances in neurology*, Vol. 8. New York, NY: Raven Press, 1995:299–321.
9. Buchtel HA, Passaro EA, Selwa LM, et al. Sodium methohexital (breivital) as an anesthetic in the Wada test. *Epilepsia* 2002;43:1056–1061.
10. Bauer PR, Reitsma JB, Houweling BM, et al. Can fMRI safely replace the Wada test for preoperative assessment of language lateralisation? A meta-analysis and systematic review. *J Neurol Neurosurg Psychiatry* 2014;85:581–588.
11. Towgood K, Barker GJ, Caceres A, et al. Bringing memory fMRI to the clinic: comparison of seven memory fMRI protocols in temporal lobe epilepsy. *Hum Brain Mapp* 2015;36:1595–1608.
12. Bonelli SB, Powell RH, Yogarajah M, et al. Imaging memory in temporal lobe epilepsy: predicting the effects of temporal lobe resection. *Brain* 2010;133:1186–1199.
13. Pelletier I, Sauerwein HC, Lepore F, et al. Non-invasive alternatives to the Wada test in the presurgical evaluation of language and memory functions in epilepsy patients. *Epileptic Disord* 2007;9:111–126.