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Muscle-Specific Differences in Neuromuscular Block and Quantitative Neuromuscular Monitoring: A Narrative Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
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Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1-3 **Paweł Radkowski**
BCDEF 4 **Dawid Kamil Malicki**
CDEF 5,6 **Florian Trachte**
CDEF 7 **Hubert Oniszczuk**

1 Department of Anesthesiology and Intensive Care, Faculty of Medicine, Collegium Medicum University of Warmia and Mazury in Olsztyn, Olsztyn, Poland
2 Department of Anaesthesiology and Intensive Care, Regional Specialist Hospital in Olsztyn, Olsztyn, Poland
3 Department of Anaesthesiology and Intensive Care, Hospital zum Heiligen Geist in Fritzlar, Fritzlar, Germany
4 Faculty of Medicine, University of Opole, Opole, Poland
5 Medical Sociology Unit, Hannover Medical School, Hannover, Germany
6 Doctor's Office, C. Zuleger Extertal, Extertal, Germany
7 Faculty of Medicine, Medical University of Białystok, Białystok, Poland

Corresponding Author: Hubert Oniszczuk, e-mail: klasa06@gmail.com

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Neuromuscular blocking agents are an essential component of contemporary anesthesiology. Adequate intraoperative neuromuscular monitoring is recommended to ensure sufficient depth of blockade and prevent postoperative residual neuromuscular block. Several quantitative techniques have been developed to assess neuromuscular transmission at the neuromuscular junction, and the number of clinically relevant monitoring sites has expanded beyond conventional peripheral muscles. In routine practice, train-of-four (TOF) stimulation combined with acceleromyography is most commonly used; the adductor pollicis serves as the standard monitoring site. However, neuromuscular responses measured at the adductor pollicis may differ from those observed in muscles critical for airway management, including the diaphragm and pharyngeal and laryngeal muscles. These muscles typically demonstrate faster onset and recovery, along with earlier recovery to TOF ratios of at least 0.9 by several minutes relative to the adductor pollicis; such dynamics have important clinical implications for intubation conditions and safe extubation. This narrative review summarizes physiologic and pharmacodynamic differences in neuromuscular block among various muscle groups and evaluates clinical evidence regarding alternative monitoring sites (eg, facial, laryngeal, pharyngeal, and foot muscles). The clinical performance and limitations of the TOF-Cuff technique applied to both the upper and lower limbs are also discussed. The review is based on clinically relevant experimental and clinical literature identified through searches of PubMed and Google Scholar, supplemented by reference screening of key papers.

Keywords: **Anesthesia, General • Muscles • Neuromuscular Blocking Agents • Neuromuscular Monitoring • Pharmacology**

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Introduction

Properly conducted general anesthesia, including the administration of neuromuscular blocking agents (NMBAs), is a key determinant of surgical conditions and perioperative safety. Early anesthetic practice relied on volatile agents such as ether, nitrous oxide, and chloroform, which provided limited and poorly controllable skeletal muscle relaxation [1]. The clinical introduction of curare represented a decisive milestone, enabling deliberate pharmacologic muscle relaxation and forming the basis for modern non-depolarizing NMBAs [2,3].

Currently available NMBAs are classified as depolarizing and non-depolarizing agents. Succinylcholine remains the only depolarizing agent in routine clinical use due to its rapid onset and short duration of action [4]. Non-depolarizing NMBAs act as competitive antagonists at the nicotinic acetylcholine receptor (nAChR) located at the neuromuscular junction [3,4].

In adult skeletal muscle, the nAChR is a pentameric ligand-gated ion channel composed of 2 $\alpha 1$ subunits, along with 1 $\beta 1$, 1 δ, and 1 ε subunit ($\alpha 1\alpha 1\beta 1\delta\varepsilon$); the ε subunit replaces the γ subunit after the neonatal period. Channel opening requires acetylcholine binding to both α subunits; neuromuscular transmission is thus a graded, receptor-dependent process, rather than an "all-or-none" phenomenon [5,6].

Quantitative neuromuscular monitoring is recommended by anesthesiology societies and is most commonly performed using train-of-four (TOF) stimulation. Objective monitoring techniques include acceleromyography (AMG), electromyography (EMG), mechanomyography, kinemyography, phonomyography, and compressomyography. Terminology has been standardized throughout the manuscript to avoid methodological ambiguity and abbreviation drift.

In routine clinical practice, neuromuscular transmission is most frequently assessed at the adductor pollicis muscle, innervated by the ulnar nerve, which remains the reference site due to its accessibility and extensive validation. However, there is increasing evidence that neuromuscular responses measured at the adductor pollicis may not fully reflect the onset, depth, or recovery of neuromuscular block within muscles directly involved in airway patency and ventilation (eg, the diaphragm and the laryngeal, pharyngeal, and selected facial muscles). These muscle-specific differences are influenced by regional perfusion, fiber-type composition, neuromuscular junction density, and the pharmacodynamic properties of individual NMBAs, as detailed in later sections of this review.

Furthermore, patient-related factors such as renal impairment can modify the clinical profile of both NMBAs and reversal drugs, strengthening the rationale for reliable quantitative monitoring across diverse perioperative populations [7]. Accordingly, this narrative review focuses on site-specific differences in neuromuscular blockade and monitoring, aiming to clarify the clinical implications of muscle-dependent responses during induction, maintenance, and recovery from general anesthesia.

Neuromuscular Conduction

A thorough understanding of acetylcholine release and motor endplate physiology is essential for both research and clinical practice in anesthesiology, particularly in the context of NMBAs. Acetylcholine is synthesized in presynaptic nerve terminals and stored in synaptic vesicles. Upon depolarization of the motor neuron and subsequent calcium influx, acetylcholine is released into the synaptic cleft, where it binds to nAChRs located on the postsynaptic membrane of skeletal muscle.

Skeletal muscle nAChRs belong to the family of ligand-gated ion channels and are pentameric in structure. As noted in the Introduction, within adult skeletal muscle, the receptor is composed of 2 $\alpha 1$ subunits, 1 $\beta 1$ subunit, 1 δ subunit, and 1 ε subunit; the ε subunit replaces the γ subunit after the neonatal period. Channel opening requires simultaneous binding of acetylcholine molecules to both α subunits, initiating depolarization of the postsynaptic membrane. Accordingly, neuromuscular transmission is a graded, receptor-dependent process, instead of an "all-or-none" phenomenon [5,6].

Non-depolarizing NMBAs exert their effects by competitively binding to acetylcholine-binding sites on the nAChR without activating the receptor. In contrast to depolarizing agents such as succinylcholine, they do not induce sustained depolarization of the motor endplate [4]. The clinical effect of neuromuscular block depends on the proportion of postsynaptic receptors occupied by the blocking agent.

During recovery, even when a substantial proportion of receptors remains blocked, sufficient acetylcholine-mediated transmission may permit muscle contraction and result in a TOF ratio approaching 0.9 despite incomplete receptor occupancy [8]. Consequently, precise quantitative intraoperative neuromuscular monitoring is essential because inaccurate assessment of neuromuscular transmission can lead to inappropriate dosing of reversal agents and increase the risk of postoperative residual neuromuscular block [6,9].

Measurement of Neuromuscular Transmission Depending on Muscle Group: The TOF Method

An ongoing challenge in clinical anesthesiology is the lack of full standardization of neuromuscular transmission measurements

Table 1. Common monitoring sites used for train-of-four (TOF) assessment and the expected observable response with preserved neuromuscular transmission.

Muscle/region (method)	Stimulated nerve	Observable response with preserved neuromuscular transmission
Corrugator supercilii muscle	Facial nerve (temporal branch)	Furrowing of the eyebrows
Orbicularis oculi muscle	Facial nerve (temporal and zygomatic branches)	Eyelid closure
Adductor pollicis muscle	Ulnar nerve (deep branch)	Adduction of the thumb
Flexor hallucis brevis muscle	Tibial nerve (medial plantar branch)	Flexion of the great toe at the metatarsophalangeal joint
Tibialis anterior muscle	Common fibular nerve	Dorsiflexion of the foot
Upper arm/forearm region (TOF-Cuff, compressomyography)	Peripheral nerves within cuff region (ulnar, median, radial, musculocutaneous)	Pressure changes induced by composite muscle contraction

TOF – train-of-four; TOF-Cuff – cuff-based compressomyography system. Facial and peripheral muscle responses and innervation patterns are derived from classical neuromuscular monitoring studies and anatomical references. Lower-limb muscle innervation and responses reflect electrophysiological and clinical monitoring data. *Sources: Monitoring site characteristics and physiological responses are summarized from published neuromuscular monitoring and anatomical literature included in this review [12,40,43,45,47].*

across different muscle groups. Individual non-depolarizing NMBAs may exhibit distinct pharmacodynamic profiles depending on the monitored muscle, a phenomenon with a multifactorial basis. Contributing factors include patient age, coexisting neurologic conditions, muscle fiber composition, regional blood flow, body temperature, and structural characteristics of the neuromuscular junction. These variables collectively influence the onset and recovery of neuromuscular block, rather than producing uniform effects across muscle groups [10].

Muscles characterized by high perfusion and a high density of postsynaptic nAChRs, such as the diaphragm and laryngeal muscles, tend to exhibit faster onset and earlier recovery of neuromuscular block, even when higher NMBA doses are required. In contrast, peripheral muscles – including the adductor pollicis muscle innervated by the deep branch of the ulnar nerve, as well as selected lower-limb muscles innervated by the tibial or common fibular nerve – typically demonstrate slower onset and more prolonged recovery of neuromuscular transmission. These site-specific differences form the physiologic rationale for muscle-dependent neuromuscular monitoring strategies [10]. Representative muscles used in clinical practice, along with their innervation and functional relevance, are summarized in **Table 1**.

In routine clinical practice, neuromuscular transmission is most commonly assessed using the TOF stimulation technique. TOF monitoring involves 4 supramaximal electrical stimuli delivered at a frequency of 2 Hz, corresponding to 0.5-second intervals between successive stimuli and a total train duration of approximately 1.5 seconds, applied to a peripheral nerve (eg, ulnar, facial, or tibial). Careful electrode placement with adequate interelectrode distance is essential because direct muscle stimulation may bypass neuromuscular transmission and substantially distort measurement results [11].

Following nerve stimulation, the evoked response of the innervated muscle group is evaluated. Typical examples include thumb adduction after ulnar nerve stimulation, reflecting activation of the adductor pollicis muscle, or brow furrowing after facial nerve stimulation, mediated by temporal branches innervating the corrugator supercilii muscle. Muscle response quantification is performed using objective monitoring techniques. AMG remains widely used but may overestimate neuromuscular recovery, particularly in the presence of patient movement or suboptimal sensor positioning [12,13].

EMG has therefore gained increasing clinical acceptance because it provides direct measurement of compound muscle action potentials and is less dependent on muscle motion or limb positioning. Although cost and device availability have historically limited EMG use, ongoing technological development is progressively addressing these barriers [14]. Portable EMG devices have also been used to quantify changes in compound muscle action potentials in critically ill, intubated patients, suggesting that EMG-based monitoring has applications beyond the operating room [15].

Assessment of neuromuscular recovery using the TOF method is based on calculation of the TOF ratio (T4/T1), defined as the amplitude of the fourth evoked response divided by the amplitude of the first evoked response. For example, a

TOF ratio of 0.7 indicates that the fourth response reaches an amplitude with 70% magnitude relative to the first response. Recommendations concerning safe extubation thresholds have substantially evolved over time. Early studies in the 1970s suggested that extubation could be safely performed at a TOF ratio of 0.7, which was revised to 0.8 in the late 1980s. Since the late 1990s, increasing evidence has consistently demonstrated that a TOF ratio of at least 0.9 is required to reliably avoid postoperative residual neuromuscular blockade and associated respiratory complications, a recommendation that remains central to contemporary anesthesiology guidelines [12,16].

In contemporary clinical cohorts, postoperative recovery of muscular function has been shown to meaningfully differ according to whether quantitative monitoring is used (AMG alone or combined approaches including ultrasonography) relative to cases without objective monitoring, reinforcing the practical relevance of routine quantitative assessment [17].

Adductor Pollicis Muscle

For several decades, the adductor pollicis muscle has been the most commonly used site for quantitative neuromuscular monitoring. This preference is largely due to the easy accessibility of its motor innervation via the deep branch of the ulnar nerve and the clearly observable mechanical response to stimulation, namely thumb adduction. Given its widespread use and extensive historical validation, the adductor pollicis muscle serves as a reference site for comparison with neuromuscular transmission measurements obtained from other muscle groups [11].

However, neuromuscular block characteristics measured at the adductor pollicis do not necessarily reflect those observed in muscles involved in airway protection. Differences in onset time, depth of block, and recovery profile have been consistently reported, limiting the direct interchangeability of measurements between the adductor pollicis and other monitoring sites. To address this limitation, investigators have proposed time-based and pharmacodynamic reference relationships, such as predictable delays or advances in recovery relative to the adductor pollicis for specific NMBAs; these relationships are discussed later in this review [18].

From a practical perspective, monitoring at the adductor pollicis may be impractical or unreliable in patients with upper-limb amputation, severe deformities, or trauma involving the hand or forearm. In such situations, alternative monitoring sites are needed to ensure accurate assessment of neuromuscular transmission during anesthesia [19].

Diaphragm

Proper diaphragmatic function is essential for effective ventilation and generation of pressure gradients between the thoracic and abdominal cavities. The diaphragm contributes approximately 70% of tidal volume during quiet breathing, underscoring the importance of accurate neuromuscular monitoring and prevention of postoperative residual neuromuscular blockade [5,20].

Anatomically, the diaphragm is a musculotendinous partition separating the thoracic and abdominal cavities; it is innervated by the phrenic nerve (C3-C5). Direct quantitative measurement of neuromuscular transmission in the diaphragm is not routinely performed in clinical practice. Experimental approaches have been described, including stimulation in the region of the anterior scalene muscle (where the phrenic nerve courses), and recording diaphragmatic responses from the seventh or eighth intercostal space [21,22].

Given its high regional blood flow and dense population of postsynaptic nAChRs, the diaphragm demonstrates pharmacodynamic characteristics that substantially differ from those of peripheral muscles [12,16,23]. Consequently, the diaphragm typically exhibits faster onset and recovery of neuromuscular blockade than peripheral muscles such as the adductor pollicis, while simultaneously demonstrating greater resistance to non-depolarizing NMBAs. Clinically, this combination complicates dosing and monitoring strategies.

Pharmacodynamic studies consistently demonstrate higher effective dose producing 50% neuromuscular block (ED50) and effective dose producing 95% neuromuscular block (ED95) values for the diaphragm compared with the adductor pollicis. Cantineau et al reported substantially higher ED50 and ED95 values for rocuronium at the diaphragm than at the adductor pollicis [22]. Similarly, Donati et al showed that complete diaphragmatic paralysis with pancuronium required approximately 2-fold higher doses than those needed at the adductor pollicis [18]. These quantitative differences explain preserved diaphragmatic activity and abdominal wall movement despite profound peripheral neuromuscular block, as determined by TOF monitoring [12,22]. Selected ED50/ED95 data and onset-recovery characteristics are summarized in **Table 2**.

Regarding reversal, multiple studies indicate that sugammadex enables more rapid recovery of diaphragmatic function after rocuronium- or vecuronium-induced blockade compared with neostigmine and may reduce postoperative pulmonary complications [24,25]. This benefit is limited by drug specificity, given that sugammadex has no effect on benzylisoquinolinium NMBAs [2]. Taken together, these findings support the need for alternative monitoring strategies or surrogate muscles that better reflect diaphragmatic neuromuscular status.

Table 2. Pharmacodynamic differences in neuromuscular blockade among muscle groups.

Neuromuscular blocking agent	Muscle group	Relative ED50/ED95 compared with adductor pollicis	Onset and recovery characteristics	Key clinical implication
Rocuronium	Diaphragm	Higher ED50 and ED95	Faster onset and faster recovery than adductor pollicis	Peripheral TOF may underestimate preserved diaphragmatic activity
Rocuronium	Adductor pollicis	Reference	Slower onset and slower recovery	Reliable site for recovery assessment
Pancuronium	Diaphragm	Approximately 2-fold higher ED50/ED95	Faster recovery despite higher dose requirement	Increased risk of residual diaphragmatic activity at peripheral TOF=0
Pancuronium	Adductor pollicis	Reference	Prolonged onset and prolonged recovery	Conventional monitoring site
Multiple NMBAs	Laryngeal muscles	Higher resistance than adductor pollicis	Rapid onset, early recovery	May explain movement or coughing despite peripheral block
Multiple NMBAs	Diaphragm	Higher resistance than peripheral muscles	Rapid onset, rapid recovery	Requires higher NMBA doses and careful reversal

ED50 – effective dose producing 50% neuromuscular block; ED95 – effective dose producing 95% neuromuscular block; NMBA – neuromuscular blocking agent; TOF – train-of-four. Relative ED50 and ED95 values indicate comparative dose requirements between muscle groups within the same study and do not represent equipotent doses across different neuromuscular blocking agents. “Faster” or “slower” onset and recovery describe temporal relationships relative to the adductor pollicis muscle under comparable anesthetic and monitoring conditions. Complete suppression of peripheral TOF responses (TOF=0) may coexist with preserved diaphragmatic or laryngeal activity. *Sources: Pharmacodynamic characteristics are summarized from comparative diaphragm, laryngeal, and peripheral muscle studies and reviews cited in the manuscript [12,16,18,22].*

In this context, facial muscles such as the orbicularis oculi or corrugator supercilii have been proposed. Additionally, diaphragm ultrasonography has emerged as a complementary tool for assessing diaphragmatic motion and recovery; although not a substitute for quantitative neuromuscular monitoring, it can provide valuable adjunctive information when performed by experienced clinicians [19,21].

Muscles of the Arm and Forearm

A more recent development in neuromuscular monitoring is the combined assessment of neuromuscular transmission and noninvasive blood pressure using the TOF-Cuff system. Unlike conventional techniques that involve selective stimulation of a single, superficially accessible peripheral nerve, TOF-Cuff monitoring relies on electrical stimulation of nerves located within the limb segment encompassed by the inflatable cuff applied to the arm [26,27].

Although the brachial plexus represents the main neural supply of the upper limb, TOF-Cuff stimulation at the arm level does not activate the plexus at its cervical origin but instead engages peripheral nerves and muscle groups located beneath the cuff, depending on cuff position, tissue impedance, and individual anatomical characteristics [28-30]. Accordingly, TOF-Cuff measurements should be interpreted as reflecting a regional, composite muscular response rather than uniform activation of all brachial plexus components [31,32].

A technical advantage of the TOF-Cuff system is its high degree of automation. The stimulating electrodes are integrated into a blood-pressure-like cuff rather than being directly applied to the skin, which may be advantageous in patients with forearm or hand deformities, extensive surgical dressings, or burns that preclude conventional electrode placement. The cuff is typically positioned on the upper arm, proximal to the elbow crease. The measurement principle utilized by TOF-Cuff is referred to as compressomyography. The device can also be applied to the lower limb, but the present section exclusively focuses on upper-limb applications.

Given the recognized limitations of adductor pollicis monitoring, several studies have evaluated TOF-Cuff as an alternative approach. In a prospective observational study involving 25 adult patients, Radkowski et al reported that, after administration of mivacurium, neuromuscular block onset measured at the arm via TOF-Cuff occurred – on average – approximately

30 seconds later than measurements obtained at the adductor pollicis muscle using TOF-Scan [31]. Based on these findings, the authors proposed a correction coefficient to facilitate clinical interpretation of TOF-Cuff measurements during induction and recovery.

Subsequent investigations have highlighted substantial interindividual variability, particularly in patients with obesity, in whom increased soft-tissue thickness may impair signal transmission and measurement reliability. In this subgroup, earlier apparent onset times – by up to approximately 60 seconds – have been reported, raising concerns about accuracy [24,32]. Conversely, in patients with a normal body mass index, TOF-Cuff measurements were broadly comparable to conventional monitoring techniques, suggesting utility in selected clinical settings.

Comparative studies have also assessed TOF-Cuff relative to facial muscle monitoring. Radkowski et al demonstrated that neuromuscular block detected at the orbicularis oculi muscle using TOF-Scan occurred earlier and resolved more rapidly than blockade measured at upper-limb muscles using TOF-Cuff [26]. Additionally, the authors noted variability depending on which upper-limb muscle groups predominantly contributed to the recorded signal, including forearm and shoulder-associated muscles, further underscoring the regional and non-uniform nature of TOF-Cuff stimulation.

Overall, the available evidence regarding upper-limb TOF-Cuff monitoring remains heterogeneous. Although the method may be useful in selected patients when conventional monitoring sites are unavailable, its performance appears limited in individuals with obesity and potentially variable across age groups, including pediatric and older patients. Current evidence is insufficient to support routine replacement of established neuromuscular monitoring techniques. Further large-scale, controlled studies are required to better define the clinical role, limitations, and interpretation of TOF-Cuff-derived measurements in upper-limb neuromuscular monitoring [24,31,32].

Orbicularis Oculi Muscle

The orbicularis oculi muscle has been investigated for its roles in anesthesiology and intensive care for more than 2 decades. Although morphologically small, it plays important physiological roles by enabling eyelid closure and protecting the ocular surface. Anatomically, the muscle is divided into orbital and palpebral parts, which slightly differ in their attachments and functional characteristics [20,33]. Functionally, the orbicularis oculi is capable of rapid, repetitive contractions that allow voluntary and reflex blinking.

This behavior is closely related to its histological composition: approximately 90% of its fibers are fast-twitch (type II), which generate rapid contractions with limited resistance to fatigue; some authors distinguish 2 subtypes within this group [12,34]. The orbicularis oculi is innervated by the temporal and zygomatic branches of the facial nerve (cranial nerve VII). The superficial course of these branches facilitates electrode placement for neuromuscular monitoring, although particular attention is needed concerning the proximity of adjacent facial muscles. Inadvertent direct muscle stimulation may distort recordings and lead to misinterpretation of neuromuscular function [20,35].

Numerous clinical studies have evaluated neuromuscular monitoring at the orbicularis oculi relative to the adductor pollicis, the conventional reference site. Whereas the adductor pollicis remains well validated for assessment of recovery, results comparing blockade onset between these 2 muscles have been heterogeneous [36,37].

In a landmark study, Ungureanu et al assessed atracurium at doses of 0.3 mg/kg and 0.5 mg/kg using AMG at both sites. Neuromuscular responses at the orbicularis oculi closely reflected blockade of the laryngeal and pharyngeal muscles, which are critical for optimal intubating conditions. Importantly, after the lower atracurium dose, incomplete laryngeal relaxation coincided with absence of blockade at the orbicularis oculi despite apparent block at the adductor pollicis, supporting its role as a surrogate for airway muscle relaxation during induction [38,39].

Subsequent studies have confirmed that neuromuscular blockade onset and early recovery occur earlier at the orbicularis oculi than at the adductor pollicis across agents such as atracurium, mivacurium, and rocuronium, with faster achievement of intermediate TOF values (eg, TOF≈0.7) at the facial site [37,40-42]. These characteristics support the use of orbicularis oculi monitoring primarily to assess blockade onset and predict intubation conditions.

In contrast, important limitations apply during recovery. Measurements at the orbicularis oculi may substantially diverge from those at peripheral muscles, and technical challenges – such as weak signal amplitude, susceptibility to artifacts, and limited applicability of some quantitative techniques – reduce reliability [42,43]. Crucially, several studies have demonstrated that a TOF ratio of 1.0 measured at the orbicularis oculi can coexist with residual neuromuscular weakness, particularly in airway and respiratory muscles, and thus does not reliably indicate safe recovery [9,22,25,44].

The orbicularis oculi is a valuable monitoring site for assessing neuromuscular blockade onset and predicting intubating conditions, especially when upper-limb monitoring is impractical.

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Table 3. Comparison of facial and peripheral monitoring sites: relationship to laryngeal adductor behavior and clinical interpretation.

Muscle monitored	Correlation with laryngeal adductor muscles	Onset of blockade vs adductor pollicis	Resistance to NMBAs	Recovery vs adductor pollicis	Reversal characteristics	Main clinical role
Corrugator supercilii	Strong	Later onset	Higher resistance	Faster recovery	Lower dose of sugammadex sufficient (eg, ~2 mg/kg)	Best facial predictor of intubating conditions
Orbicularis oculi	Moderate	Earlier onset	Moderate resistance	Faster recovery	TOF=1.0 may occur with residual block	Useful for onset only; unsafe for extubation
Adductor pollicis	Poor (airway muscles)	Reference	Lower resistance	Slowest recovery	Requires higher reversal doses	Gold standard for recovery and extubation

NMBA – neuromuscular blocking agent; TOF – train-of-four. Correlation with laryngeal adductor muscles primarily refers to similarity in onset and early recovery of neuromuscular blockade. Recovery at facial sites occurs earlier than recovery at peripheral muscles and does not reliably reflect restoration of pharyngeal or airway-protective muscle function. A TOF ratio of 1.0 measured at the orbicularis oculi does not exclude residual neuromuscular weakness. *Sources: Evidence is summarized from clinical comparative studies evaluating facial, laryngeal, and peripheral monitoring sites and reversal characteristics [38,47,48,50].*

However, due to limited reliability during recovery, it should not be used to guide extubation decisions. Confirmation of adequate recovery should be performed at a peripheral muscle, such as the adductor pollicis, using quantitative monitoring and a TOF ratio of at least 0.9 [9,25].

Corrugator Supercilii Muscle

The corrugator supercilii muscle is the second major facial-nerve-innervated site investigated for neuromuscular monitoring. Despite its small size, its superficial location in the medial eyebrow region allows reliable detection of facial nerve stimulation, typically expressed as vertical forehead wrinkling. Anatomically, the muscle lies superior to the orbicularis oculi and consists of 2 bellies (oblique and transverse) with slightly different fiber orientation and attachments [20,34,35].

Histologically, the corrugator supercilii contains a balanced mixture of type I and type II muscle fibers, in contrast to the predominantly fast-twitch profile of the orbicularis oculi. This mixed fiber composition explains its intermediate sensitivity to non-depolarizing NMBAs and its closer physiological resemblance to the laryngeal adductor muscles [12,34,45].

A substantial body of literature has compared neuromuscular responses of the corrugator supercilii, orbicularis oculi, and adductor pollicis to identify the most reliable site for predicting the onset and depth of neuromuscular blockade [12,45,46]. In a pivotal 2001 study, Plaud et al showed that after rocuronium 0.5 mg/kg, neuromuscular responses at the corrugator supercilii closely mirrored those of the laryngeal adductor muscles; responses at the orbicularis oculi resembled those at the adductor pollicis. Later onset and faster early recovery at the corrugator supercilii reflected the known resistance of laryngeal musculature to NMBAs [45,47].

Subsequent studies have consistently demonstrated that, compared with monitoring at peripheral muscles, monitoring at the corrugator supercilii provides a more accurate prediction of laryngeal relaxation during induction, facilitating optimal timing of tracheal intubation. Importantly, laryngeal relaxation – and corrugator supercilii paralysis – does not necessarily coincide with relaxation of the tongue or pharyngeal muscles, which remain critical determinants of postoperative airway safety [44,48].

Differences between the corrugator supercilii and peripheral muscles also extend to reversal of neuromuscular blockade. Suzuki et al reported that maintaining a comparable depth of block required higher rocuronium infusion rates at the corrugator supercilii than at the orbicularis oculi, consistent with greater resistance to NMBAs. After neostigmine administration, recovery to a TOF ratio of 0.9 occurred substantially faster at the corrugator supercilii than at the adductor pollicis, further supporting its similarity to laryngeal adductors [38,49].

Comparable findings were reported by Yamamoto et al, who demonstrated that after rocuronium 1 mg/kg, reversal at the corrugator supercilii required only 2 mg/kg of sugammadex; reversal at the adductor pollicis required nearly twice that dose under identical conditions [50]. Radkowski et al evaluated upper-arm TOF-Cuff monitoring relative to conventional TOF-Scan measurements at the adductor pollicis; in a separate study, they performed a comparison with eyelid monitoring to reflect facial nerve stimulation during mivacurium anesthesia [26,31]. Although these studies did not directly assess the corrugator supercilii muscle, they underscore the composite and region-dependent nature of cuff-based measurements, which limits direct extrapolation to specific facial muscles.

Collectively, current evidence supports the corrugator supercilii as an excellent predictor of the onset and depth of neuromuscular blockade at the laryngeal adductor muscles, particularly when upper-limb monitoring is impractical. However, its recovery occurs considerably earlier than that of the adductor pollicis, and it does not reliably reflect pharyngeal or tongue muscle function. Consequently, the corrugator supercilii should not be used to guide extubation decisions. Technical challenges related to electrode placement, small signal amplitude, and proximity to adjacent facial muscles further limit its role during recovery [9,12,20,25,35,44,45]. A comparative summary of facial and peripheral monitoring sites, including onset characteristics, resistance to NMBAs, recovery patterns, and clinical implications, is presented in **Table 3**.

Laryngeal Muscles

The larynx is a complex structure due to its muscular organization and highly coordinated functional mechanisms. Laryngeal muscles are classically divided into extrinsic and intrinsic groups. From an anesthesiologist's perspective, the intrinsic muscles – arytenoid, thyroarytenoid, lateral cricoarytenoid, posterior cricoarytenoid, and cricothyroid – are of primary importance.

Innervation of the laryngeal muscles is provided by branches of the vagus nerve (cranial nerve X), but the pattern is not uniform. All intrinsic laryngeal muscles, except the cricothyroid muscle, are innervated by the recurrent laryngeal nerve. The cricothyroid muscle is exclusively innervated by the external branch of the superior laryngeal nerve. Both the lateral and posterior cricoarytenoid muscles, which play key roles in vocal fold adduction and abduction, receive motor innervation solely from the recurrent laryngeal nerve [51,52].

From a histological perspective, laryngeal muscles exhibit a very high density of neuromuscular junctions and a substantial proportion of type II (fast-twitch) muscle fibers, particularly among intrinsic muscles. These characteristics contribute to their specific pharmacodynamic profile, including a relatively rapid onset and faster recovery from neuromuscular blockade compared with peripheral muscles [12,16]. Similar to the diaphragm, laryngeal muscles are relatively resistant to non-depolarizing NMBAs and therefore often require higher effective concentrations to achieve complete paralysis [12,21].

Multiple studies have demonstrated that the neuromuscular blockade characteristics of the laryngeal muscles closely resemble characteristics observed at the corrugator supercilii muscle, although they substantially differ from measurements obtained at the adductor pollicis muscle [12,45,47]. This observation underlies the clinical rationale for using facial-nerve-innervated muscles as indirect indicators of laryngeal muscle relaxation during anesthesia.

Direct monitoring of laryngeal muscles remains challenging due to their deep anatomical location and the course of the recurrent laryngeal nerve. Nevertheless, direct approaches have been explored. One study utilized laryngeal EMG involving electrodes integrated into the endotracheal tube, combined with transcutaneous stimulation of the recurrent laryngeal nerve. After administration of mivacurium or rocuronium, the duration of neuromuscular blockade was consistently shorter at the laryngeal muscles than at the adductor pollicis, supporting previously reported muscle-specific differences [53]. The authors emphasized, however, that inadvertent direct muscle stimulation may generate falsely reassuring measurements.

Earlier invasive techniques, including needle electrode insertion into vocal cord muscles or recordings obtained through laryngeal cartilages, were investigated in the past but did not gain widespread acceptance due to limited feasibility and safety concerns; they are no longer used in routine clinical practice [52].

Differences between laryngeal and peripheral muscles are also evident during pharmacological reversal of neuromuscular blockade. Pavoni et al demonstrated earlier recovery of laryngeal muscle function compared with the adductor pollicis; however, their approach utilized sugammadex 16 mg/kg to reverse profound neuromuscular block, defined as deep suppression of neuromuscular transmission [54]. This method differs from that of studies addressing moderate block. For example, Yamamoto et al showed that sugammadex 2 mg/kg was sufficient to reverse moderate neuromuscular blockade, assessed at the corrugator supercilii muscle, which exhibits pharmacodynamic behavior similar to that of the laryngeal muscles [50]. These findings indicate that apparent discrepancies in sugammadex dosing reflect differences in the depth of neuromuscular block and predefined reversal endpoints, rather than true physiological inconsistencies.

Overall, peripheral muscles such as the adductor pollicis or lower-limb muscles do not reliably reflect neuromuscular transmission at the laryngeal level. Accurate assessment of laryngeal muscle relaxation is crucial to minimize airway-related complications, including aspiration. Thus, further development of validated indirect monitoring strategies or direct measurement techniques remains an important objective in contemporary anesthesiology [9,12,25,45,54].

Pharyngeal Muscles

Proper pharyngeal muscle function is essential for effective swallowing and airway protection, thereby reducing the risk of postoperative complications such as aspiration pneumonia [9]. This function relies on highly coordinated neuromuscular control with complexity comparable to that of the laryngeal muscles, underscoring its vulnerability during and after general anesthesia.

The pharyngeal musculature comprises elevator muscles (stylopharyngeus and palatopharyngeus) as well as the superior, middle, and inferior pharyngeal constrictors, which act as sphincters. Motor innervation of the pharyngeal muscles is complex but follows well-defined anatomical principles. The majority of pharyngeal muscles receive motor fibers via the pharyngeal plexus, primarily formed by branches of the glossopharyngeal nerve (cranial nerve IX) and the vagus nerve (cranial nerve X). The stylopharyngeus muscle is exclusively innervated by the glossopharyngeal nerve (IX), whereas most other pharyngeal muscles are supplied through vagal fibers within the pharyngeal plexus. The accessory nerve (cranial nerve XI) does not provide direct motor innervation to the pharyngeal muscles but contributes indirectly via its association with the vagus nerve [51,55].

From a pharmacodynamic perspective, pharyngeal muscles exhibit neuromuscular block characteristics similar to those of the laryngeal muscles, including relatively rapid neuromuscular blockade onset and earlier recovery compared with peripheral muscles such as the adductor pollicis [12,16]. Despite this tendency for earlier recovery, clinically relevant pharyngeal dysfunction may persist even when peripheral monitoring suggests adequate neuromuscular recovery.

Fuchs-Buder et al demonstrated that at TOF ratios of approximately 0.8, substantial impairment of pharyngeal muscle function may persist, compromising swallowing and airway protection [48,56]. This phenomenon is particularly relevant for muscles such as the geniohyoid, whose relaxation can result in posterior displacement of the tongue and subsequent airway obstruction. Although the geniohyoid muscle demonstrates rapid neuromuscular blockade onset similar to that of central muscle groups, its recovery may be unexpectedly prolonged, in some cases approaching recovery times observed at the adductor pollicis [48,57].

Pharyngeal muscle function is especially critical in older patients, among whom age-related decline in muscle strength and coordination further increases susceptibility to postoperative aspiration [58]. Overall, pharyngeal muscles demonstrate neuromuscular block behavior that substantially differs from the behavior of peripheral muscles and closely resembles that of the laryngeal muscles or diaphragm [12,16,48]. These differences highlight the limitations of solely relying on peripheral neuromuscular monitoring to assess recovery of airway-protective function and emphasize the need for cautious interpretation of TOF values during emergence from anesthesia.

TOF-Cuff Measurements on the Lower Leg

The TOF-Cuff technique, originally introduced for use on the arm and forearm muscles, has also been evaluated for neuromuscular transmission monitoring in the lower limb. The fundamental principle of the method remains unchanged, enabling simultaneous assessment of neuromuscular block and noninvasive blood pressure.

Lower-limb TOF-Cuff measurements primarily involve muscles innervated by the tibial nerve, which is stimulated within the region enclosed by the cuff. The tibial nerve is a terminal branch of the sciatic nerve and separates in the popliteal fossa, accompanying the popliteal vessels. Distally, it passes through the tarsal tunnel and divides into the medial and lateral plantar nerves. Muscles supplied by the tibial nerve include the tibialis posterior, flexor digitorum longus, soleus, and flexor hallucis longus [20,59].

Compared with upper-limb applications, substantially less data are available regarding TOF-Cuff use on the lower limb, a situation that reflects both the limited routine use of lower-limb muscles for neuromuscular monitoring and the relative novelty of this approach [59-62]. Consequently, lower-limb TOF-Cuff measurements should be interpreted in relation to established reference techniques, particularly ulnar nerve monitoring with TOF-Scan, which remains the most extensively validated method [9,25,27,63].

A prospective observational study by Radkowski et al compared neuromuscular blockade measurements at the adductor pollicis muscle using TOF-Scan with measurements obtained from lower-limb muscles using TOF-Cuff during mivacurium anesthesia [60]. Contrary to initial expectations, the timing of neuromuscular blockade onset was nearly identical at both sites, confirming prior observations [26,61,62]. In contrast, recovery of neuromuscular transmission occurred substantially faster in muscles innervated by the tibial nerve than at the adductor pollicis [59,60]. The mechanisms underlying these differences remain uncertain and may include small sample size and interindividual variability related to age or obesity. In addition to neuromuscular transmission, Radkowski et al reported discrepancies in diastolic blood pressure measurements, which are clinically relevant given the known hemodynamic effects of NMBAs [60].

A comparable observational study was published by Dullenkopf et al in 2020, evaluating TOF-Cuff placement on the lower leg during anesthetic induction [61]. In that study, atracurium was used after induction with propofol and fentanyl, and blood pressure was reported as mean arterial pressure. Complete neuromuscular blockade (TOF=0) occurred earlier at the adductor pollicis, although delays exceeding 60 seconds were observed in some patients. Neuromuscular measurements could not be obtained in approximately 20% of patients, highlighting technical limitations of the method.

Also in 2020, Chau et al compared TOF-Scan measurements on the upper limb with TOF-Cuff measurements on the lower limb during modified rapid-sequence induction using atracurium [62]. Although mean onset times did not significantly differ, large interindividual variability was observed; differences exceeded 100 seconds in some cases and no consistent direction favored either technique.

Taken together, current evidence does not support routine use of TOF-Cuff on lower limbs [60-62]. Although average values may approximate those obtained using TOF-Scan, substantial variability related to patient-specific factors – including obesity, calf circumference, age, and soft-tissue coverage of the tibial nerve – might result in clinically relevant discrepancies [59-61]. Thus, lower-limb TOF-Cuff monitoring should be regarded as an adjunct technique, useful in selected clinical scenarios rather than as a standard method [10,27]. Further validation in larger and more heterogeneous patient populations is required before routine clinical implementation can be recommended [9,25,60-63].

Foot Muscles

Foot muscles have been explored as alternative sites for quantitative neuromuscular monitoring, mainly via stimulation of the posterior tibial nerve and recording responses from intrinsic foot muscles. This approach may be useful when upper-limb access is limited; however, site-specific pharmacodynamic differences mean that measurements at the foot can diverge from those obtained at the adductor pollicis and must be interpreted cautiously [12,16].

One clinically studied pathway is the posterior tibial nerve-flexor hallucis brevis configuration. In a multicenter prospective trial, Chen et al evaluated the feasibility and agreement of this foot-site approach against standard adductor pollicis monitoring using TOF stimulation; their results demonstrated that reliable measurements are possible in selected patients but that onset and recovery characteristics may differ between sites [59]. Differences between hand and foot TOF responses have also been reported in intraoperative neurophysiologic monitoring contexts, supporting the hypothesis that limb location and local tissue conditions can influence the observed neuromuscular response [64].

Importantly, earlier apparent recovery at the foot does not guarantee adequate restoration of upper-airway protective muscle function. Current consensus documents and reviews emphasize that extubation safety should be based on quantitative confirmation of recovery at a validated peripheral site, most commonly the adductor pollicis, with a TOF ratio of at least 0.9 [9,25,63,65]. Because postoperative residual neuromuscular blockade remains clinically relevant and is associated with adverse respiratory outcomes, foot monitoring should be regarded as an adjunct, rather than a replacement for standard monitoring strategies [25,66,67].

Discussion

Physicians and researchers currently have access to a broad spectrum of tools for quantitative neuromuscular transmission monitoring, reflecting decades of progress in anesthesiology. Historically, assessment of neuromuscular block evolved in parallel with general anesthesia, from early inhalational agents to the introduction of curare and modern non-depolarizing NMBAs [1-3,68]. Despite technological advances, TOF stimulation remains the most widely used and guideline-endorsed method for assessing neuromuscular block [9,25].

TOF can be combined with objective techniques such as AMG, EMG, mechanomyography, kinemyography, phonomyography, and compressomyography, the latter additionally allowing noninvasive blood pressure measurement [8,10,43,65]. As noted in the Introduction, terminology has been standardized throughout this manuscript to avoid methodological ambiguity. Although quantitative techniques have improved precision, full standardization across monitoring sites has not been achieved [63,65].

A consistent finding across experimental and clinical studies is that the onset, depth, and recovery of neuromuscular block are muscle-specific and influenced by perfusion, fiber composition, neuromuscular junction density, and NMBA pharmacodynamics [12,16,58]. In routine practice, the adductor pollicis muscle, innervated by the deep branch of the ulnar nerve, remains the reference site because of its accessibility and extensive validation. A TOF ratio of at least 0.9 at the adductor

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pollicis is accepted as the benchmark for recovery prior to extubation [9,25,63,65].

However, increasing evidence indicates that responses at the adductor pollicis do not reliably reflect neuromuscular function of airway and respiratory muscles, including the diaphragm and the laryngeal and pharyngeal muscles [12,16,25,44,67]. In the diaphragm, studies consistently show higher ED50 and ED95 values, in some cases approaching 2-fold higher doses than at the adductor pollicis, along with faster onset and earlier recovery [12,16,18,22]. These findings highlight the physiological limitations of peripheral monitoring when extrapolated to respiratory muscles [12,16,25,67].

Facial muscles, particularly the orbicularis oculi, have been proposed as alternative sites for assessing intubating conditions. Several studies demonstrated closer correlations with laryngeal muscle relaxation than with measurements at the adductor pollicis, especially during neuromuscular block onset [37,39,40,46]. This behavior is likely related to fiber composition and perfusion, rather than anatomical proximity alone [12,16]. Important limitations must be emphasized because reliable AMG measurements at the orbicularis oculi heavily depend on electrode placement, avoidance of direct muscle stimulation, and operator experience [42,43,63].

Facial nerve stimulation may also activate adjacent muscles, including the corrugator supercilii, which – although technically more challenging – has been shown to track laryngeal adductor behavior more closely, particularly during neuromuscular block onset and early recovery [38,45,50]. Pharyngeal and laryngeal muscles, essential for airway protection and swallowing, exhibit neuromuscular characteristics most closely resembling those of the diaphragm. Multiple studies have indicated that recovery considered adequate at the adductor pollicis can coexist with clinically relevant pharyngeal dysfunction. In this context, a TOF ratio of 0.8 may be insufficient because pharyngeal weakness and impaired swallowing can persist, increasing the risk of aspiration [48,56,67].

The TOF-Cuff system represents a recent approach enabling neuromuscular monitoring in the upper and lower limbs with simultaneous blood pressure measurement. However, stimulation through a cuff activates regional nerves within the cuffed segment; published data reveal substantial interindividual variability, particularly in patients with obesity or atypical limb morphology [24,26,27,31,32,60-62]. Furthermore, TOF-Cuff measurements are not consistently correlated with facial muscle responses, limiting their role as a replacement for established standards [26,31].

Foot muscles, innervated by the tibial nerve and its branches, have also been investigated. Although they may show earlier recovery than the adductor pollicis, this recovery must not be used to guide extubation because it may underestimate residual weakness of airway-protective muscles [9,64,67]. Accordingly, foot muscle monitoring should be regarded only as an adjunct when conventional sites are unavailable [9,14,59,64].

In our view, integration of the available evidence indicates that quantitative monitoring at the adductor pollicis – preferably using EMG – remains the most reliable method for confirming recovery and ensuring extubation safety. Facial muscle monitoring may provide valuable information regarding neuromuscular block onset and intubation conditions, particularly when upper-limb monitoring is impractical. Other monitoring sites should currently be considered supportive rather than substitutive, pending further high-quality comparative studies. Continued research will likely refine future recommendations and promote more individualized neuromuscular monitoring strategies [15].

Future Directions

Future research should focus on refining site-specific neuromuscular monitoring strategies, rather than seeking a single universal measurement location. Facial muscles such as the corrugator supercilii and orbicularis oculi appear to reflect laryngeal muscle behavior during neuromuscular block onset more accurately than peripheral muscles, supporting their further evaluation as predictive sites for intubation conditions. Additional standardized studies are required to define their optimal role within induction-phase monitoring algorithms.

Direct monitoring of muscles critical for airway protection remains technically challenging but represents an important research direction. Advances in stimulation and signal acquisition technologies may enable more reliable assessment of neuromuscular transmission in respiratory and airway-related muscles, thus improving intraoperative decision-making without reliance on indirect indicators alone.

Cuff-based monitoring systems such as TOF-Cuff show potential as adjunctive tools, particularly when access to conventional monitoring sites is limited. However, their clinical applicability remains restricted by interindividual variability, reduced reliability in patients with obesity, and inconsistent correlations with facial and respiratory muscle responses. Large-scale, multicenter studies are necessary to determine their true clinical value and assess whether site- or patient-specific correction factors can be developed. Investigations should also address quantitative conversion models between monitoring sites. Establishment of validated relationships between peripheral measurements and neuromuscular function of airway-protective muscles could support more individualized monitoring strategies while preserving patient safety. Finally, diaphragmatic ultrasonography represents a promising complementary modality for intraoperative assessment of respiratory muscle function. Although ultrasound-based evaluation might enhance understanding of diaphragmatic mechanics during neuromuscular block and recovery, its role remains investigational. Prospective validation in diverse patient populations is needed before integration into routine monitoring standards.

Conclusions

Quantitative neuromuscular monitoring remains a cornerstone of safe anesthetic practice and effective prevention of postoperative residual neuromuscular blockade. This narrative review demonstrates that neuromuscular block is inherently muscle-specific, with substantial differences in onset, depth, and recovery between peripheral muscles and those critical for airway patency and ventilation, such as the diaphragm and the laryngeal and pharyngeal muscles.

Despite these physiological differences, monitoring at the adductor pollicis muscle remains the most reliable and best-validated method for confirming adequate recovery before extubation. A TOF ratio of at least 0.9 measured at this site, preferably using EMG, should continue to be regarded as the clinical standard for extubation safety.

Facial muscles, particularly the orbicularis oculi and corrugator supercilii, provide valuable information regarding neuromuscular block onset and intubation conditions; they may better reflect laryngeal muscle behavior during induction. However, these muscles should not be used alone to assess recovery. Alternative monitoring sites such as lower-limb and foot muscles, as well as cuff-based technologies, may serve as adjuncts in selected clinical situations but currently lack sufficient consistency to replace established reference methods. Earlier recovery at peripheral or distal sites must not be used to guide extubation decisions because it may underestimate residual weakness in airway-protective muscles. In summary, optimal neuromuscular monitoring requires a site- and phase-specific approach: facial muscles for prediction of intubating conditions and quantitative monitoring at the adductor pollicis for confirmation of recovery. Until further high-quality comparative studies are available, these principles should guide clinical practice to minimize respiratory complications and enhance perioperative safety.

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References:

1. Radkowski P, Mazuchowski M, Opolska J, et al. History of striated muscle relaxants used in anaesthesiology. Farm Pol. 2024;80(6):367-74
2. Renew JR, Brull SJ. Clinical pharmacology of drugs acting at the neuromuscular junction. In: Basic Sciences in Anesthesia. Springer; 2025;147-67
3. Bowman WC. Neuromuscular block. Br J Pharmacol. 2006;147(Suppl. 1):S277-86
4. Karunarathna I, Tharayil AS. Understanding atracurium: a guide to neuromuscular blockade [Internet]. Uva Clinical Lab; 2024 [cited 2026 Feb 14]. Available from: https://www.academia.edu/download/122827619/Understanding_Atracurium.pdf
5. Martyn JAJ, Jonsson Fagerlund M, Eriksson LI. Basic principles of neuromuscular transmission. Anaesthesia. 2009;64(Suppl. 1):1-9
6. Radkowski P, Dawidowska-Fidrych J, Fidrych R, et al. Postoperative residual curarization as a complication after general anesthesia. Pol Ann Med. 2022;29(2):274-80
7. Radkowski P, Krupiniewicz KJ, Suchcicki M, et al. Navigating anesthesia: Muscle relaxants and reversal agents in patients with renal impairment. Med Sci Monit. 2024;30:e945141
8. Understanding neuromuscular monitoring [Internet]. [cited 2026 Feb 14]. Available from: https://www.amhsr.org/articles/understanding-neuromuscular-monitoring-11226.html
9. Naguib M, Brull SJ, Kopman AF, et al. Consensus statement on perioperative use of neuromuscular monitoring. Anesth Analg. 2018;127(1):71-80
10. Lee W. The latest trend in neuromuscular monitoring: Return of the electromyography. Anesth Pain Med (Seoul). 2021;16(2):133-37
11. Oh SK, Park S, Lim BG, et al. Comparison between the trapezius and adductor pollicis muscles as an acceleromyography monitoring site for moderate neuromuscular blockade during lumbar surgery. Sci Rep. 2021;11(1):14568
12. Hemmerling TM, Donati F. Neuromuscular blockade at the larynx, the diaphragm and the corrugator supercilii muscle: A review. Can J Anaesth. 2003;50(8):779-94
13. Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. Anesthesiology. 2008;109(3):389-98
14. Radkowski P, Grond S, Brunner H, et al. Comparison of relaxometry between ulnar nerve and posterior tibial nerve after cisatracurium administration using electromyography. Anesth Pain Med. 2023;13(1):e132866
15. Greenberg SB, Locke AR, Ben-Isvy N, et al. A pilot study using a portable electromyography device to assess changes in compound muscle action potential amplitudes and latencies in critically ill intubated patients. Anesthesiology. 2026;144(3):715-19
16. Fuchs-Buder T. Pharmacodynamics of neuromuscular blocking agents in different muscle groups. Curr Anesthesiol Rep. 2025;15(1):9
17. Huang S, Pan Y, Wang Y, et al. Muscular function recovery from general anesthesia in 132 patients undergoing surgery with acceleromyography, combined acceleromyography, and ultrasonography, and without monitoring muscular function. Med Sci Monit. 2024;30:e942780
18. Donati F, Meistelman C, Plaud B. Vecuronium neuromuscular blockade at the diaphragm, the orbicularis oculi, and adductor pollicis muscles. Anesthesiology. 1990;73(5):870-75
19. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. Muscle Nerve. 2013;47(3):319-29
20. Standring S, Ellis H, Healy J, et al. Gray's anatomy: The anatomical basis of clinical practice. 39th ed. Edinburgh: Elsevier Churchill Livingstone; 2005
21. Sun Y, Sun S, Chen R, et al. Diaphragm ultrasonography as a monitor in assessing antagonistic effect of sugammadex on rocuronium in patients with Child-Pugh grades A and B. Front Med (Lausanne). 2024;11:1370021

22. Cantineau JP, Porte F, D'Honneur G, Duvaldestin P. Neuromuscular effects of rocuronium on the diaphragm and adductor pollicis muscles in anesthetized patients. Anesthesiology. 1994;81(3):585-90
23. Tayar ASA, Abdelshafey EE. Diaphragm electromyography versus ultrasonography in the prediction of mechanical ventilation liberation outcome. Respir Care. 2022;67(11):1437-42
24. Markle A, Graf N, Horn K, Welter JE, Dullenkopf A. Neuromuscular monitoring using TOF-Cuff® versus TOF-Scan®: An observational study under clinical anesthesia conditions. Minerva Anestesiol. 2020;86(7):704-11
25. Murphy GS, Brull SJ. Quantitative neuromuscular monitoring and postoperative outcomes: A narrative review. Anesthesiology. 2022;136(2):345-61
26. Radkowski P, Ruść J, Kęska M, Sztaba K. Comparing neuromuscular blockade measurement between upper arm (TOF Cuff®) and eyelid (TOF Scan®) using mivacurium during general anesthesia. Med Sci Monit. 2024;30:e943630
27. Kameyama Y, Takagi S, Seto K, et al. Efficiency of the TOF-Cuff™ for the evaluation of rocuronium-induced neuromuscular block and its reversal with sugammadex: A comparative study vs. acceleromyography. J Anesth. 2019;33(1):80-84
28. Orebaugh SL, Williams BA. Brachial plexus anatomy: Normal and variant. ScientificWorldJournal. 2009;9:300-12
29. Leinberry CF, Wehbé MA. Brachial plexus anatomy. Hand Clin. 2004;20(1):1-5
30. Bayot ML, Nassereddin A, Varacallo MA. Anatomy, shoulder and upper limb, brachial plexus. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Feb 14]. Available from: https://pubmed.ncbi.nlm.nih.gov/29763192/
31. Radkowski P, Ruść J, Kęska M. Comparison of measurements obtained with TOF-Cuff placed on the arm and the TOF-Scan on the adductor pollicis muscle during general anaesthesia using mivacurium: a prospective observational clinical trial. Sci Rep. 2024;14(1):27180
32. Markle A, Horn K, Welter JE, Dullenkopf A. An observational study comparing the performance of TOF-Cuff with TOF-Scan monitoring during anaesthetic induction in clinical routine. Anaesthesiol Intensive Ther. 2020;52(3):181-86
33. Tong J, Lopez MJ, Fakoya AO, Patel BC. Anatomy, head and neck: orbicularis oculi muscle. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Feb 14]. Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK441907/
34. Goodmurphy CW, Ovalle WK. Morphological study of two human facial muscles: Orbicularis oculi and corrugator supercilii. Clin Anat. 1999;12(1):1-11
35. Yang H, Kim HJ. Anatomical study of the corrugator supercilii muscle and its clinical implication with botulinum toxin A injection. Surg Radiol Anat. 2013;35(9):817-21
36. Caffrey RR, Warren ML, Becker KE. Neuromuscular blockade monitoring comparing the orbicularis oculi and adductor pollicis muscles. Anesthesiology. 1986;65(1):95-97
37. Rimaniol JM, Dhonneur G, Sperry L, Duvaldestin P. A comparison of the neuromuscular blocking effects of atracurium, mivacurium, and vecuronium on the adductor pollicis and the orbicularis oculi muscle in humans. Anesth Analg. 1996;83(4):808-13
38. Suzuki T, Mizutani H, Miyake E, et al. Infusion requirements and reversibility of rocuronium at the corrugator supercilii and adductor pollicis muscles. Acta Anaesthesiol Scand. 2009;53(10):1336-40
39. Ungureanu D, Meistelman C, Frossard J, Donati F. The orbicularis oculi and the adductor pollicis muscles as monitors of atracurium block of laryngeal muscles. Anesth Analg. 1993;77(4):775-79
40. Le Corre F, Plaud B, Benhamou E, Debaene B. Visual estimation of onset time at the orbicularis oculi after five muscle relaxants: Application to clinical monitoring of tracheal intubation. Anesth Analg. 1999;89(5):1305-10
41. Abdulatif M, El-Sanabary M. Blood flow and mivacurium-induced neuromuscular block at the orbicularis oculi and adductor pollicis muscles. Br J Anaesth. 1997;79(1):24-28
42. Larsen PB, Gätke MR, Fredensborg BB, et al. Acceleromyography of the orbicularis oculi muscle II: comparing the orbicularis oculi and adductor pollicis muscles. Acta Anaesthesiol Scand. 2002;46(9):1131-36
43. Radkowski P, Barańska A, Mieszkowski M, et al. Methods for clinical monitoring of neuromuscular transmission in anesthesiology – A review. Int J Gen Med. 2024;17:9-20
44. Fuchs-Buder T, Nemes R, Schmartz D. Residual neuromuscular blockade: Management and impact on postoperative pulmonary outcome. Curr Opin Anaesthesiol. 2016;29(6):662-67
45. Plaud B, Debaene B, Donati F. The corrugator supercilii, not the orbicularis oculi, reflects rocuronium neuromuscular blockade at the laryngeal adductor muscles. Anesthesiology. 2001;95(1):96-101
46. Lee HJ, Kim KS, Jeong JS, et al. Comparison of the adductor pollicis, orbicularis oculi, and corrugator supercilii as indicators of adequacy of muscle relaxation for tracheal intubation. Br J Anaesth. 2009;102(6):869-74
47. Meistelman C, Plaud B, Donati F. Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. Can J Anaesth. 1992;39(7):665-69
48. Cedborg AIH, Sundman E, Bodén K, et al. Pharyngeal function and breathing pattern during partial neuromuscular block in the elderly: Effects on airway protection. Anesthesiology. 2014;120(2):312-25
49. Jiang R, Horvath B. Neostigmine. In: The essence of analgesia and analgesics. Cambridge University Press; 2010;479-81
50. Yamamoto S, Yamamoto Y, Kitajima O, et al. Reversal of neuromuscular block with sugammadex: A comparison of the corrugator supercilii and adductor pollicis muscles in a randomized dose-response study. Acta Anaesthesiol Scand. 2015;59(7):892-901
51. Noordzij JP, Ossoff RH. Anatomy and physiology of the larynx. Otolaryngol Clin North Am. 2006;39(1):1-10
52. Kartush JM, Naumann IC. Laryngeal nerve monitoring. Neurodiagn J. 2014;54(3):227-59
53. Hemmerling TM, Schurr C, Walter S, et al. A new method of monitoring the effect of muscle relaxants on laryngeal muscles using surface laryngeal electromyography. Anesth Analg. 2000;90(2):494
54. Pavoni V, Gianesello L, Martinelli C, et al. Recovery of laryngeal nerve function with sugammadex after rocuronium-induced profound neuromuscular block. J Clin Anesth. 2016;33:14-19
55. Sakamoto Y. Classification of pharyngeal muscles based on innervations from glossopharyngeal and vagus nerves in human. Surg Radiol Anat. 2009;31(10):755-61
56. d'Hollander AA, Bourgain JL. [Residual curarization and pharyngeal muscles: remain vigilant!] Ann Fr Anesth Reanim. 2009;28(10):868-77 [in French]
57. D'Honneur G, Guignard B, Slavov V, et al. Comparison of the neuromuscular blocking effect of atracurium and vecuronium on the adductor pollicis and the geniohyoid muscle in humans. Anesthesiology. 1995;82(3):649-54
58. Radkowski P, Kowalczyk K, Łęczycka A, et al. Age-specific pharmacology of neuromuscular blocking agents: A comprehensive review. Med Sci Monit. 2025;31:e949656
59. Chen W, Chen Z, Cheng F, et al. The feasibility of the posterior tibial nerve-flexor hallucis brevis pathway applied in neuromuscular monitoring: A multicentric, controlled, and prospective clinical trial. PeerJ. 2024;12:e17154
60. Radkowski P, Ruść J, Kęska M. Evaluation of neuromuscular blockade: A comparative study of TOF-Cuff® on the lower leg and TOF-Scan® on the ulnar nerve during mivacurium anesthesia. Med Sci Monit. 2024;30:e945227
61. Dullenkopf A, Horn K, Steurer MP, et al. Placement of TOF-Cuff® on the lower leg for neuromuscular and blood pressure monitoring during anesthetic induction for shoulder surgeries. J Anesth. 2020;34(1):79-85
62. Chau I, Horn K, Dullenkopf A. Neuromuscular monitoring during modified rapid sequence induction: A comparison of TOF-Cuff® and TOF-Scan®. Australas Emerg Care. 2020;23(4):217-20
63. Fuchs-Buder T, Brull SJ, Fagerlund MJ, et al. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents III: The 2023 Geneva revision. Acta Anaesthesiol Scand. 2023;67(8):994-1017
64. Gavrancic B, Lolis A, Beric A. Train-of-four test in intraoperative neurophysiologic monitoring: differences between hand and foot train-of-four. J Clin Neurophysiol. 2014;31(6):575-79
65. Grabarczyk Ł. Advances in neuromuscular monitoring techniques in anesthesiology: A 2025 perspective. Med Sci Monit. 2025;31:e948980
66. Piersanti A, Garra R, Sbaraglia F, et al. Neuromuscular monitoring and incidence of postoperative residual neuromuscular blockade: A prospective observational study. J Anesthesia Analg Crit Care. 2025;5(1):5
67. Blum FE, Locke AR, Nathan N, et al. Residual neuromuscular block remains a safety concern for perioperative healthcare professionals: A comprehensive review. J Clin Med. 2024;13(3):861
68. Rahman MM, Basta T, Teng J, et al. Structural mechanism of muscle nicotinic receptor desensitization and block by curare. Nat Struct Mol Biol. 2022;29(4):386-94