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Objective parameters to measure (in)stability of the knee joint during gait: A review of literature

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ABSTRACT

Background: Instability of the knee joint during gait is frequently reported by patients with knee osteoarthritis or an anterior cruciate ligament rupture. The assessment of instability in clinical practice and clinical research studies mainly relies on self-reporting. Alternatively, parameters measured with gait analysis have been explored as suitable objective indicators of dynamic knee (in)stability.
Research question: This literature review aimed to establish an inventory of objective parameters of knee stability during gait.
Methods: Five electronic databases (Pubmed, Embase, Cochrane, Cinahl and SPORTDiscuss) were systematically searched, with keywords concerning knee, stability and gait. Eligible studies used an objective parameter(s) to assess knee (in)stability during gait, being stated in the introduction or methods section. Out of 10717 studies, 89 studies were considered eligible.
Results: Fourteen different patient populations were investigated with kinematic, kinetic and/or electromyography measurements during (challenged) gait. Thirty-three possible objective parameters were identified for knee stability, of which the majority was based on kinematic (14 parameters) or electromyography (12 parameters) measurements. Thirty-nine studies used challenged gait (i.e. external perturbations, downhill walking) to provoke knee joint instability. Limited or conflicting results were reported on the validity of the 33 parameters.
Significance: In conclusion, a large number of different candidates for an objective knee stability gait parameter were found in literature, all without compelling evidence. A clear conceptual definition for dynamic knee joint stability is lacking, for which we suggest : “The capacity to respond to a challenge during gait within the natural boundaries of the knee”. Furthermore biomechanical gait laboratory protocols should be harmonized, to enable future developments on clinically relevant measure(s) of knee stability during gait.

1. Introduction

Instability of the knee joint is a frequent occurring problem during dynamic daily activities in patients with knee osteoarthritis (KOA) or anterior cruciate ligament injury (ACL) [1,2]. Patients perceive knee joint instability as a sensation of buckling, shifting or giving way of the joint [3–5]. In the KOA population 63–76% of the patients report these sensations [2,6,7]. In addition, higher pain levels and lower physical function are reported in patients with self-reported ‘unstable’ knees compared to patients with self-reported ‘stable’ knees [8–10]. Severe pain and knee joint instability could cause patients to change their movement patterns, for example by stiffening their knee through greater **co**-contraction of the muscles [8,11]. These alterations might lead to a-typical loading of the joint, which could have a negative

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influence on the progression of diseases like KOA [11,12]. Likewise, instability related injuries such as ACL ruptures will change joint kinematics, and consequently cartilage load, increasing the risk of developing KOA at a later stage [13,14]. Knee joint instability should therefore be considered in the management of (early) KOA.

Generally accepted objective metrics to assess knee joint instability are still lacking [15,16]. This absence of a valid objective measure of (in)stability makes it difficult to evaluate the outcome of conservative interventions and to design prevention strategies for those at risk of knee joint instability. Currently, knee joint instability has been described via self-reported outcomes [17], static and passive measurements of knee laxity [18] or postural balance tests [19]. Unfortunately, none of these methods objectively quantifies knee stability during daily activities (i.e. gait, stair climbing, turning) in which knee joint stability is often reported [2,10]. Gait analysis enables biomechanical quantification of knee function, opening the possibility to measure dynamic knee joint stability. Some of the objective metrics measured with gait analysis are now suggested to express dynamic knee joint stability [11,20–23]. For instance, greater knee flexion angle excursions during gait were measured in patients with KOA and complaints of joint instability compared to those without complaints [16]. Along with the kinematic and kinetic parameters, neuromechanical parameters during gait are also considered. For example higher **co**-contraction values were observed in the injured leg of ACL-patients compared to their uninjured leg [24]. Gait analysis might therefore be a suitable measurement tool to identify objective parameter(s) that could assist in the diagnostics of knee instability in patients.

Gait analysis is frequently performed at comfortable gait (i.e. comfortable gait speed, solid ground, without external influences), but since this might be accompanied by compensating knee instability it would need a challenge to reveal “true” knee joint instability. Therefore studies have been looking at challenged gait as a candidate to investigate dynamic knee joint stability [21,25,26]. As dynamic knee stability sometimes is defined as the ability to recover from external perturbations [23,25,27], well controlled challenges might be used to represent the moments where knee joint stability is put to test during daily life. Challenged gait might be for instance a downhill walkway [28], changing gait speeds [29] or adding mechanical external perturbations by the use of a movable platform [30]. Besides challenging the task, also advanced data processing methods are used to express stability of the knee [27,31,32]. An example of this is calculating apparent knee joint stiffness, that combines the knee extensor moment with the knee flexion-extension angle, assuming patients increase knee joint stiffness to overcome knee joint instability [33]. Another example is the Lyapunov exponent which uses the full time series of the measured knee angle(s) during gait to express instability of the knee joint [32]. An overview of all the various objective gait parameters of knee (in)stability that are currently used to measure knee joint stability will inform the direction for development of a reliable and clinically relevant (valid) objective measure for dynamic knee (in)stability. Such a measure will enhance the evaluation of therapies that target knee joint instability (e.g. exercising muscle strength [34] or the application of knee braces [35]) in patient populations with KOA or ACL injury. Therefore, the aim of this literature review was to establish an inventory of the objective parameters used for knee stability during gait.

2. Methods

2.1. Search strategy

Five electronic databases were searched on August 9th, 2016 for eligible studies: Pubmed, Embase, Cochrane Library, CINAHL and SPORTDiscuss. An update of the search was performed on January 10th, 2018 for the inclusion of additional eligible studies. The search strategy included keywords concerning (I) knee, (II) instability, (III) gait. The first two keywords (I and II) were searched on title and abstract. The last keyword (III) was searched on full text. A language filter on English was added. Reference tracking of the reference lists of the included eligible studies was performed to avoid missing eligible studies. The search strategy used for the electronic databases is presented below:

1. Knee joint OR Knee OR Genu OR Tibiofibular OR Tibiofibular Joint
2. Instability OR Stability OR Joint instability OR Balance OR Support OR Steadiness OR Unsteadiness OR Firmness OR Sturdiness OR Unstableness OR Insecurity OR Confidence OR Buckling OR Giving way OR Shifting OR Stiffness
3. Locomotion OR Walk OR Walking OR Gait OR Step OR March OR Pace OR Stride OR Ambulate OR Ambulation
4. #1 AND #2 AND #3
5. #4 AND English[lang]

2.2. Study eligibility criteria

A study was considered eligible when an objective parameter(s) to measure knee joint instability during gait was used, which was stated in the introduction or methods section of the article. Case, animal and model-based studies were excluded, as well as review articles, non-English written articles and conference abstracts.

2.3. Study selection

The search resulted in 10717 studies, which were imported into a citation manager. Duplicates were removed. Title and abstract were screened by one author (JS) and resulted in 545 studies. Two authors (JS and JN) independently performed the full text screening, and discussions were resolved with the help of a third author (ME). Reference tracking added 5 eligible studies. A total of 89 eligible studies were finally included in this review (5 studies were from the update). In Fig. 1 the selection procedure is presented.

2.4. Data extraction

The following data were extracted by one author (JS) from the studies: author, year of publication, sample size, number of healthy subjects, patient population, experimental setup, type of gait, type of perturbations, objective parameter(s) used to measure knee (in)stability and the key results related to the research topic. The objective parameters extracted were mentioned in the introduction or methods section as parameter for knee joint (in)stability. The study group was defined as the patient group or the leg having knee joint instability. Comfortable gait was defined as walking at one constant gait speed, on a solid level walkway and without external perturbations from the environment.

3. Results

The literature search resulted in 89 eligible studies [6–9,11,15,16,20–23,25,26,28,30–33,36–104]. The characteristics of the eligible studies are presented in Table 1. The average sample size was 37 subjects and 14 different patient populations were studied. The three main patient populations investigated were anterior cruciate ligament (ACL) injuries (30%), knee osteoarthritis (27%) and **trans**-tibial amputees (4%). In 22% of studies, only healthy subjects were included. Primarily kinematics (36%) were measured in the studies, 24% also included kinetics and 21% used a combination of kinematics, kinetics and electromyography (EMG). Solely EMG was used in 10% of the studies and a small portion of the studies used a different combination (7% kinematics & EMG and 2% kinetics & EMG). Measurement of challenged gait was performed in 44% of the studies, of these, 31% used external perturbations in the form of a moveable platform, (visual) obstacle or an instability shoe (in healthy subjects, patients with an ACL injury or KOA). Fig. 2 provides the overview of the 33 objective

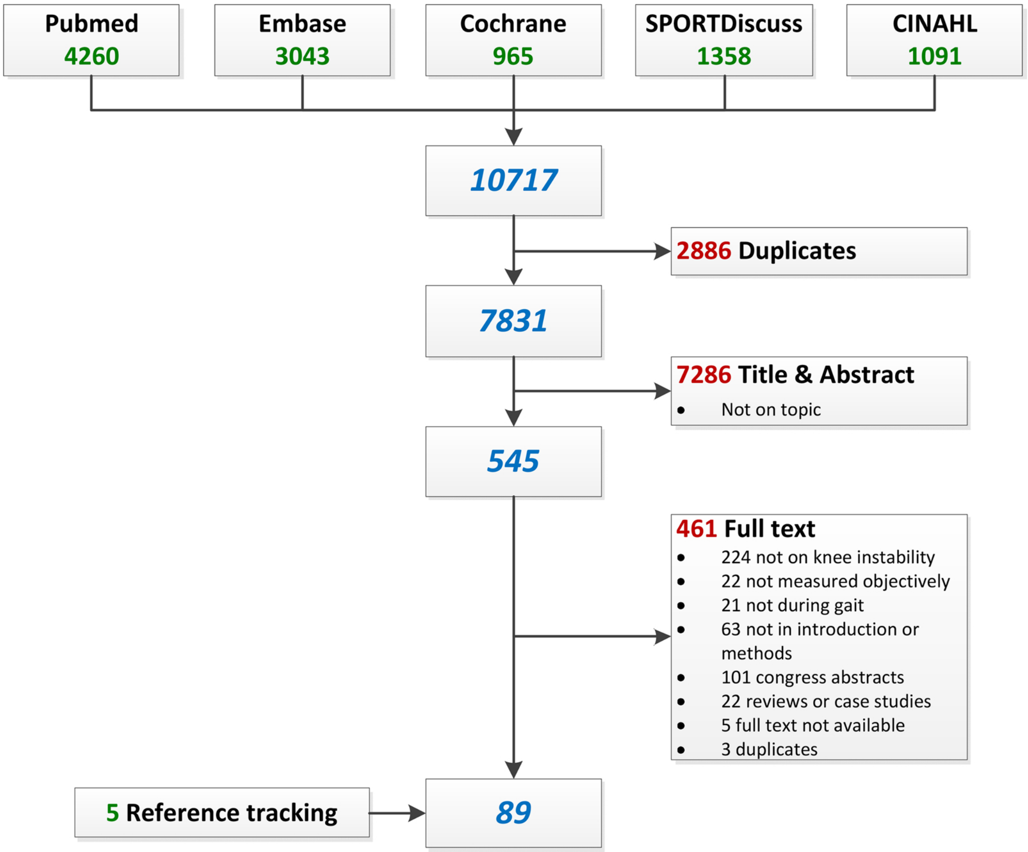

Fig. 1. Overview of the selection procedure.

parameters used for the measurement of dynamic knee joint stability during gait. The objective parameters were categorized by either kinematics, kinetics, EMG or a combination of those, and then sorted by frequency of reporting in the studies. Tables 2 and 3 present the objective parameters used during comfortable gait and challenged gait, alongside study information, methodology and key findings. Only the objective parameters that were used in more than 5% of the studies or were highlighted as novel by the authors are presented in this result section.

3.1. Knee flexion angle

Patients with knee joint instability are thought to have altered knee movement patterns during gait compared to healthy subjects and patients with "stable" knees. The knee flexion angle was therefore explored as objective parameter for knee joint stability in 25% of all studies (22 studies), during comfortable gait (Table 2, 12 studies) and challenged gait (Table 3, 10 studies). Four types of patient populations (patients with an ACL injury, KOA, cerebellar ataxia and chronic instability patients) were measured with marker-based recordings of the kinematics. The knee flexion angle was often defined in the studies as the peak flexion angle (PK), flexion excursion (FE), flexion angle at heel strike (FAH) or flexion angle at mid-stance (FMS). During comfortable gait seven studies observed an altered PK, FE, FAH or FMS in the study group [8,20,24,61,76,88], three studies reported differences between patients with ACL-S (patients with an ACL injury and self-reported "stable" knees) and control subjects [36,48,76] and two studies reported no differences between groups [63,82]. During challenged gait five studies reported differences in flexion angles (PK, FE, FAH, FMS or flexion angle during terminal stance phase) between the study group and control group [21,26,72,87,104], two studies did not observe a difference [16,99] and one study showed a lower PK and higher PK standard deviation (during perturbation) in patients with ACL-S compared to control subjects [50]. Two studies investigated the effect of instability shoes and observed changes in knee flexion angle (FE, PK) [37,64]. Change in gait speed did not affect the result in two out of three studies [99,104] and Kumar et al. [72] showed that patients with KOA had similar responses in knee flexion angle to external perturbations compared to controls [72].

3.2. Maximal finite-time Lyapunov

The maximal finite-time Lyapunov represents the variability in joint angles (caused by small natural occurring perturbations) during normal walking, in which a higher Lyapunov exponent indicates a higher variability in the movement of the knee i.e. a more unstable knee [84]. The maximal finite-time Lyapunov exponent was used in 18% of all studies as objective parameter for knee joint stability (16 studies), during comfortable gait (Table 2, 5 studies) and challenged gait (Table 3, 11 studies). Studies investigated patients with an ACL injury, KOA, an amputation, cerebral palsy (CP), Parkinson's disease, peripheral neuropathy, peripheral arterial and healthy subjects (seven different patient populations). The complete time series of the 3D knee angles or solely of the knee flexion angle were used as input for the calculation. During comfortable gait three studies observed higher Lyapunov exponents in the study group compared to the control group (s) [46,74,84]. Wearing a safety harness [55] or arm swing [102] did not have an influence on the Lyapunov exponents of the knee in healthy subjects. During challenged gait higher Lyapunov exponents were reported in the injured leg of patients with an ACL injury (compared with the uninjured leg) [32], the uninjured leg ofpatients with KOA (compared to control subjects) [29] and in the dominant leg of children with cerebral palsy (compared to the non-dominant leg) [45]. Two studies did not observe a difference in Lyapunov exponents [81,92] and two

Table 1
Characteristics of the eligible studies.

Study Characteristics

Author & publication year	Sample size	Healthy subjects	Patient population	Measurement method	Type of Gait	Objective parameters
Alkjaer et al. 2003	38	19	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, amplitude of muscle activation, co-activation index
Apps et al. 2016	18	18	No	Kinematics, kinetics, EMG	Challenged gait (instability shoes)	Knee flexion angle, knee flexion – extension moment, knee joint stiffness, amplitude of muscle activation, co-contraction index
Arellano et al. 2009	23	23	No	Kinematics	Challenged gait (load carrying)	Maximum Floquet multiplier
Beard et al. 1996	27	9	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, duration of muscle activition
Beaudette et al. 2015	12	12	No	Kinematics	Challenged gait (load carrying)	Maximal finite-time Lyapunov
Boerboom et al. 2001	10	0	ACL	Kinematics, EMG	Challenged gait (change in walking speed)	Deviation index
Boeth et al. 2013	21	8	ACL	Kinematics	Comfortable gait	Tibiofemoral anterior-posterior translation
Bohn et al. 2015	61	16	ACL	Kinematics, kinetics	Comfortable gait	Tibial rotation
Boudarham et al. 2016	25	11	Multiple sclerosis	Kinematics, kinetics, EMG	Comfortable gait	Co-activation index, co-activation duration
Bulea et al. 2017	20	10	Cerebral palsy	Kinematics	Challenged gait (load carrying)	Maximal finite-time Lyapunov
Buzzi et al. 2003	20	20	No	Kinematics	Comfortable gait	Maximal finite-time Lyapunov
Centomo et al. 2007	12	6	Amputees	Kinematics, kinetics, EMG	Comfortable gait	Co-contraction index
Chang et al. 2013	236	0	Knee osteoarthritis	Kinematics, kinetics	Comfortable gait	Varus-valgus movement
Chmielewski et al. 2001	21	10	ACL	Kinematics, kinetics	Comfortable gait	Knee flexion angle, knee flexion – extension moment, ground reaction forces, total support moment
Chmielewski et al. 2002	9	0	ACL	EMG	Comfortable gait	Amplitude of muscle activation, muscle onset time
Chmielewski et al. 2005	34	17	ACL	Kinematics, EMG	Challenged gait (moveable platform)	Knee flexion angle, co-contraction index
Claes et al. 2011	30	10	ACL	Kinematics	Comfortable gait	Tibial rotation
Collins et al. 2014	34	17	Knee osteoarthritis	Kinematics, kinetics, EMG	Comfortable gait	Co-contraction index, knee joint stiffness
da Fonseca et al. 2004	20	10	ACL	EMG	Challenged gait (moveable platform)	Co-contraction ratio
da Fonseca et al. 2006	36	36	No	EMG	Comfortable gait	Co-contraction ratio
Debbi et al. 2012	10	10	No	Kinematics, kinetics	Challenged gait (instability shoe)	Variability index
Decker et al. 2012	10	10	No	Kinematics	Comfortable gait	Maximal finite-time Lyapunov
Dingwell et al. 2007	37	23	Peripheral Neuropathy	Kinematics	Comfortable gait	Maximum Floquet multiplier
Donker and Beek 2002	14	7	Amputees	Kinematics	Challenged gait (change in walking speed)	Relative phase dynamics
Fallah-Yakhdani et al. 2010	28	12	Knee Osteoarthritis	Kinematics	Challenged gait (change in walking speed)	Maximal finite-time Lyapunov
Fallah-Yakhdani et al. 2012	43	27	Knee Osteoarthritis	Kinematics, EMG	Challenged gait (change in walking speed)	Maximal finite-time Lyapunov, co-contraction time
Fantini Pagani et al. 2013	12	0	Knee Osteoarthritis	EMG	Comfortable gait	Amplitude of muscle activation, co-contraction ratio
Farrokhi et al. 2012	26	12	Knee Osteoarthritis	Kinematics, kinetics	Challenged gait (downhill walking)	Knee flexion angle, 3D knee angles, 3D knee translations
Farrokhi et al. 2014	43	25	Knee Osteoarthritis	Kinematics, kinetics	Challenged gait (downhill walking)	Knee flexion angle, 3D knee angles, knee contact point movement
Farrokhi et al. 2015	53	0	Knee Osteoarthritis	Kinematics, kinetics	Comfortable gait	Knee flexion angle, knee flexion – extension moment, total support moment
Farrokhi et al. 2016	22	11	Knee Osteoarthritis	Kinematics, kinetics	Challenged gait (downhill walking)	Varus-valgus movement, knee contact point movement
Fuentes et al. 2011	44	15	ACL	Kinematics, kinetics	Challenged gait (change in walking speed)	Knee flexion angle, knee rotational moment
Galli et al. 2017	79	18	Cerebral Palsy	Kinematics, kinetics	Comfortable gait	Knee joint stiffness
Gardinier et al. 2012	31	0	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, Modeling muscle forces
Gustafson et al. 2015	43	24	Knee Osteoarthritis	Kinematics, kinetics	Challenged gait (downhill walking)	Variability index
Gustafson et al. 2016	52	0	Knee Osteoarthritis	Kinematics, kinetics	Comfortable gait	Knee flexion angle, knee flexion – extension moment, knee joint stiffness
Hooper et al. 2002	18	9	Chronic Posterior Instability	Kinematics, kinetics	Comfortable gait	Knee flexion angle, knee flexion – extension moment

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Table 1 (*continued*)

Study Characteristics						
Horsak and Baca 2013	12	12	No	Kinematics, kinetics, EMG	Challenged gait (perturbation shoe)	Knee flexion angle, knee flexion – extension moment, ground reaction forces, amplitude of muscle activation
Hortobagyi et al. 2005	46	20	Knee Osteoarthritis	Kinetics, EMG	Comfortable gait	Amplitude of muscle activation, co-activation ratio
Hubley-Kozey et al. 2006	78	38	Knee Osteoarthritis	Kinematics, kinetics, EMG	Comfortable gait	Principal Component Analysis (PCA)
Hurd and Snyder-Mackler 2007	21	0	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, total support moment, Amplitude of muscle activation, co-contraction index
Hurmuzlu et al. 1996	26	9	Post-Polio	Kinematics	Comfortable gait	Maximum Floquet multiplier
Hutin et al. 2011	29	15	Hemiparesis	Kinematics, kinetics, EMG	Comfortable gait	Relative phase dynamics
Jones et al. 1983	16	10	ACL	Kinematics	Comfortable gait	3D knee angles
Kalund et al. 1990	15	6	ACL	Kinetics, EMG	Challenged gait (uphill walking and change in walking speed)	Muscle onset time
Khan et al. 2013	45	18	Knee Arthroplasty	Kinematics	Comfortable gait	Knee accelerations
Kumar et al. 2013	61	23	Knee Osteoarthritis	Kinematics, EMG	Challenged gait (moveable platform)	Knee flexion angle, amplitude of muscle activation
Kurz et al. 2005	20	10	ACL	Kinematics	Comfortable gait	Relative phase dynamics
Kurz et al. 2010	30	25	Parkinson	Kinematics	Comfortable gait	Maximal finite-time Lyapunov
Kvist 2004	20	0	ACL	Kinematics	Comfortable gait	Tibiofemoral anterior-posterior translation
Lewek et al. 2002	38	10	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, amplitude of muscle activation
Lewek et al. 2006	30	15	Knee Osteoarthritis	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, co-contraction index, variability index
Li et al. 2005	5	5	No	Kinematics	Challenged gait (virtual perturbation and change in walking speed)	Perturbation recovery time
Lu et al. 2008	15	15	No	Kinematics	Challenged gait (obstacle)	Relative phase dynamics
Lustosa et al. 2011	25	0	ACL	EMG	Challenged gait (moveable platform)	Co-contraction index
Mahmoudian et al. 2016	43	27	Knee Osteoarthritis	Kinematics	Challenged gait (change in walking speed)	Maximal finite-time Lyapunov
Manor et al. 2008	24	12	Peripheral Neuropathy	Kinematics	Challenged gait (change in walking speed)	Maximal finite-time Lyapunov
Mari et al. 2014	34	17	Cerebellar Ataxia	Kinematics, EMG	Comfortable gait	Knee flexion angle, amplitude of muscle activation, co-activation index
Matic et al. 2016	35	0	ACL	Kinematics	Comfortable gait	Tibiofemoral anterior-posterior translation, tibial rotation
Morgan et al. 2016	32	16	ACL	Kinematics, kinetics	Comfortable gait	Nyquist and Bode criteria
Myers et al. 2009	36	17	Peripheral Arterial	Kinematics	Comfortable gait	Maximal finite-time Lyapunov
Obuchi et al. 1999	30	30	No	Kinematics	Comfortable gait	Tibiofemoral anterior-posterior translation
Ramsey et al. 2007	16	0	Knee Osteoarthritis	Kinematics, kinetics, EMG	Comfortable gait	Co-contraction index
Roberts et al. 2013	45	18	Knee Arthroplasty	Kinematics	Comfortable gait	Knee accelerations
Rudolph et al. 1998	16	0	ACL	Kinematics, kinetics	Challenged gait (obstacle)	Knee flexion angle, knee flexion – extension moment, ground reaction forces
Rudolph et al. 2001	31	10	ACL	Kinematics, kinetics, EMG	Comfortable gait	Knee flexion angle, knee flexion – extension moment, ground reaction forces, total support moment, amplitude of muscle activation, muscle onset time, duration of muscle activation
Russell and Haworth 2014	10	10	No	Kinematics	Challenged gait (change in stride frequency)	Maximal finite-time Lyapunov
Russell et al. 2016	10	10	No	Kinematics	Challenged gait (load carrying)	Maximal finite-time Lyapunov
Schmitt and Rudolph 2008	20	0	Knee Osteoarthritis	Kinematics, EMG	Challenged gait (moveable platform)	Co-contraction index
Segal et al. 2008	19	19	No	Kinematics	Challenged gait (turning gait)	Maximal finite-time Lyapunov
Segal et al. 2010	10	0	Amputees	Kinematics	Challenged gait (turning gait)	Maximal finite-time Lyapunov
Seyedali et al. 2012	14	5	Amputees	EMG	Challenged gait (change in walking speed)	Co-contraction area
Sharma et al. 2015	212	0	Knee Osteoarthritis	Kinematics, kinetics	Comfortable gait	Varus – valgus movement
Sharma et al. 2017	44	0	Knee Osteoarthritis	EMG	Comfortable gait	Amplitude of muscle activation, co-contraction ratio, co-activation ratio
Sinkjaer et al. 1991	30	16	ACL	EMG	Challenged gait (uphill walking)	Amplitude of muscle activation, muscle onset time, duration of muscle activation
Skou et al. 2014	100	0	Knee Osteoarthritis	Kinematics, kinetics	Comfortable gait	Varus-valgus movement

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Table 1 (*continued*)

Study Characteristics						
Stastny et al. 2014	16	16	No	Kinematics, kinetics, EMG	Challenged gait (load-carrying)	Co-contraction ratio, muscle onset time, co-activation ratio
Stergiou et al. 2004	10	0	ACL	Kinematics	Challenged gait (change in walking speed)	Maximal finite-time Lyapunov
Sturnieks et al. 2011	119	30	Meniscectomy	Kinematics, kinetics, EMG	Comfortable gait	Amplitude of muscle activation, co-contraction ratio
Tagesson et al. 2013	130	130	No	Kinematics	Comfortable gait	Tibiofemoral anterior-posterior translation
Tibone et al. 1986	20	0	ACL	Kinematics, kinetics, EMG	Challenged gait (change in walking speed)	Knee flexion angle, ground reaction forces, amplitude of muscle activation
Turcot et al. 2009	33	9	Knee Osteoarthritis	Kinematics	Comfortable gait	Knee accelerations
van der Esch et al. 2008	63	0	Knee Osteoarthritis	Kinematics, kinetics	Comfortable gait	Varus-valgus movement
van den Noort et al. 2017	9	9	No	Kinematics, kinetics	Challenged gait (moveable treadmill)	Gait Sensitivity Norm (GSN)
Winby et al. 2009	11	11	No	Kinematics, kinetics, EMG	Challenged gait (change in walking speed)	Modeling muscle forces
Wu et al. 2016	24	24	No	Kinematics	Comfortable gait	Maximal finite-time Lyapunov
Yamashita et al. 1999	6	6	No	EMG	Comfortable gait	Amplitude of muscle activation
Yim et al. 2014	35	0	ACL	Kinematics, kinetics	Challenged gait (change in walking speed)	Knee flexion angle, tibiofemoral anterior-posterior translation, 3D knee angles
Zeni and Higginson 2009	56	22	Knee Osteoarthritis	Kinematics, kinetics	Challenged gait (change in walking speed)	Knee joint stiffness

studies presented lower Lyapunov exponents in the study group compared to control [15,29]. Challenging gait by load-carrying [40,45,90] or change in stride frequency [89] led to higher Lyapunov exponents in the knee of healthy subjects and children with cerebral palsy. Change of gait speed resulted in different Lyapunov exponents between groups in two out of the six studies [29,81]. Turning gait led to higher Lyapunov exponents in healthy subjects [91], but not in amputees [92]. At last, Fallah-Yakhdani et al. [58] showed that Lyapunov exponents were a predictor for **co-**contraction time of the muscles surrounding the knee.

3.3. *Tibiofemoral anterior – posterior translation*

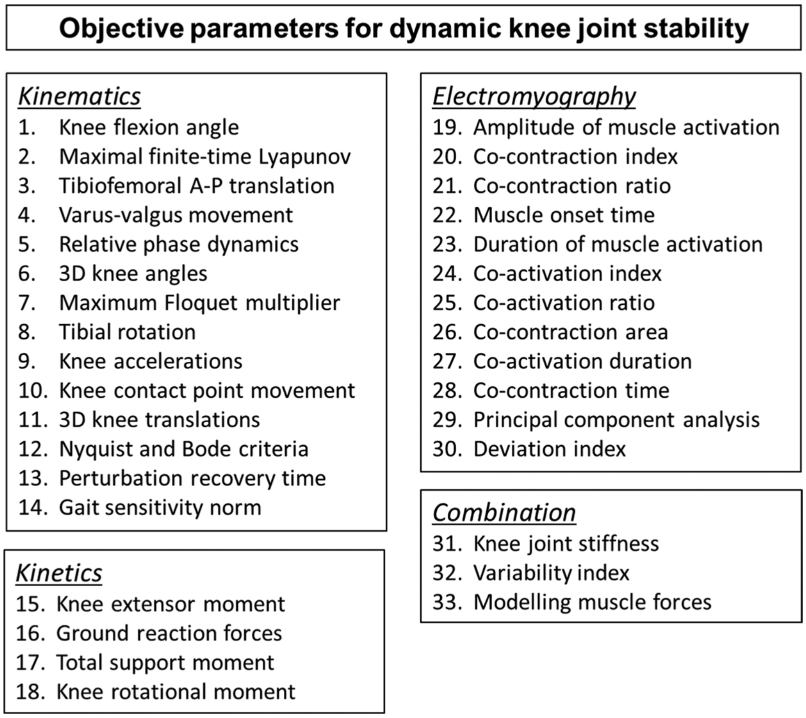
Tibiofemoral anterior – posterior (a-p) translation is often greater in patients with an ACL injurycompared to control when measured with passive laxity tests [42], but it remains unknown how these patients stabilize the translation during active movements. Therefore, it was investigated in 7% of all studies as an objective parameter for knee joint stability, during comfortable gait (Table 2, 5 studies) and challenged gait (Table 3,1 study). The kinematics of patients with an ACL injury and healthy subjects were obtained using marker-based recordings or potentiometers. The tibiofemoral a-p translation was defined in the studies as the mean (MT), range of translation (RT) or maximum (MAT). During comfortable gait three studies observed lower tibiofemoral a-p translation (MT, RT, MAT) in the injured leg of patients with an ACL injurycompared to the uninjured leg (or post-surgery) [42,75,83]. No differences were reported in tibiofemoral a-p translation (MT & MAT) between the legs of healthy subjects [85] and Tagesson et al. [98] reported that women had higher MAT values than men. During challenged gait, lower MT was observed in the ACL injured leg compared to the uninjured leg at two gait speeds (no difference between gait speeds) [104].

3.4. *Varus – valgus movement*

Varus- valgus movement is minimal in healthy subjects, therefore it is assumed that greater varus-valgus movement in patients might be an indicator of instability [23]. For that reason, 6% of all studies used varus-valgus movement as objective parameter for knee joint stability, during comfortable gait (Table 2, 4 studies) and challenged gait (Table 3,1 study). Patients with KOA were investigated with the use of marker-based recordings or Dynamic Stereo X-ray recordings (and additional CT-images) of the kinematics. Dynamic Stereo X-ray is a measurement in which subjects walk on a treadmill surrounded with a biplane X-ray system to capture the movement of the knee [28]. The studies defined the varus-valgus movement as varus-valgus excursion (VVE), varus excursion (VE), maximum varus angle during loading response (MV) or maximum varus-valgus angular velocity (MVVV). During comfortable gait a higher MV and MVVV was observed in patients with KOA and (observed) varus thrust compared to patients with KOA and without varus thrust [22], but no difference was observed in VVE and MVV between patients with KOA-I and KOA-S [9]. Additionally, higher varus – valgus movement during comfortable gait was shown to be associated with knee confidence [7] and independent of joint laxity, muscle strength, skeletal alignment and knee joint proprioception [23]. During challenged gait (downhill walking), higher VE was observed in patients with KOA compared to control subjects [28].

3.5. *Knee flexion-extension moment*

Knee flexion-extension moment is thought to be altered in patients with instability (by for example **co-**contraction of the muscles or a shift of the load distribution to other joints) and was used in 15% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2, 10 studies) and challenged gait (Table 3,3 studies). The studies included patients with KOA, an ACL injury and posterior instability or healthy subjects. The knee flexion-extension moment was



Objective parameters for dynamic knee joint stability

Kinematics
1. Knee flexion angle
2. Maximal finite-time Lyapunov
3. Tibiofemoral A-P translation
4. Varus-valgus movement
5. Relative phase dynamics
6. 3D knee angles
7. Maximum Floquet multiplier
8. Tibial rotation
9. Knee accelerations
10. Knee contact point movement
11. 3D knee translations
12. Nyquist and Bode criteria
13. Perturbation recovery time
14. Gait sensitivity norm

Kinetics
15. Knee extensor moment
16. Ground reaction forces
17. Total support moment
18. Knee rotational moment

Electromyography
19. Amplitude of muscle activation
20. Co-contraction index
21. Co-contraction ratio
22. Muscle onset time
23. Duration of muscle activation
24. Co-activation index
25. Co-activation ratio
26. Co-contraction area
27. Co-activation duration
28. Co-contraction time
29. Principal component analysis
30. Deviation index

Combination
31. Knee joint stiffness
32. Variability index
33. Modelling muscle forces

Fig. 2. Overview of the objective parameters for dynamic knee joint stability during gait. (3D = three-dimensional, a-p = Anterior – Posterior).

measured using force plates and motion capture. It was defined as the peak extensor moment (PK), peak flexion moment (PF) or the moment at initial knee extension (EI). During comfortable gait six studies observed an altered knee flexion-extension moment (PE, PF, EI) in the study group versus controls [8,24,61,76,77,88], however, four studies did not report this difference [20,36,48,63]. During challenged gait a lower PF was reported in the injured legs of patients with ACL-I (patients with an ACL injury and self-reported “unstable” knees) and patients with ACL-S compared to their uninjured leg [87]. Instability shoes did not influence the knee flexion-extension moment (PE and PF) [37,64].

3.6. Ground reaction forces

Ground reaction forces are thought to be lower in patients with knee instability as a strategy to (together with stiffening of the knee) try to stabilize the knee during walking [87]. Ground reaction forces were used in 6% of the studies as objective parameter for knee joint stability, during comfortable gait (Table 2,2 studies) and challenged gait (Table 3,3 studies). Patients with an ACL injury and healthy subjects were measured using force plates. During comfortable gait and challenged gait the ground reaction forces were lower in patients with ACL-I and ACL-S compared to control [48,87,88]. No differences in ground reaction forces were observed due to change in gait speed in patients with ACL-I [99]. An instability shoe was found to increase the ground reaction forces in healthy subjects [64].

3.7. Amplitude of muscle activation

Patients with knee joint instability are suggested to have a neuromuscular adaption to compensate for the instability of the joint. The amplitude of muscle activation was therefore used in 18% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2, 11 studies) and challenged gait (Table 3, 5 studies). The patient populations measured (with the use of electromyography) in the studies were patients with KOA, an ACL injury, cerebellar ataxia or Arthroscopic Partial Meniscectomy (APM) or healthy subjects. The studies used different normalization procedures for the amplitude of muscle activation (for example: to maximal voluntary contraction or peak at level walking) or expressed the amplitude of muscle activation as the Root Mean Square (RMS), the Average Rectified Value (ARV) or integral of the loading response phase (IL). During comfortable gait, five studies presented alterations in muscle activation (Il, ARV, RMS) between the study group and control group [24,82,88,94,97], but three studies did not [36,65,76]. After perturbation training, higher vastus lateralis IL activation was observed in patients with an ACL injury [49]. Fantini Pagani et al. [59] showed that braces were able to lower muscle activations (RMS) in patients with KOA [59]. Yamashita et al. [103] suggested that high muscle activity in the vastus medialis could be a sign of instability during gait. During challenged gait, three studies observed alterations in amplitude of muscle activations due to uphill walking [95] or the use of an instability shoe [37,64]. Kumar et al. [72] reported higher lateral hamstring activation in patients with KOA (compared to control) during level and perturbed walking. Varying the gait speed resulted in no difference in amplitude of muscle activation in the legs patients with ACL-I [99].

3.8. Co-contraction index

Patients with knee joint instability are presumed to counteract knee instability by higher **co**-contraction of the muscles surrounding the knee. The **co**-contraction index was used in 10% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2, 5 studies) and challenged gait (Table 3, 4 studies). The investigated patient populations were patients with KOA, an ACL injury or an amputation or healthy subjects. As input for the calculation of the **co**-contraction index the muscle activations of several muscles surrounding the knee were used. During comfortable gait, two studies observed higher **co**-contraction indices in the study group compared to the control group [24,77], one study did not show a difference [52] and one study reported lower **co**-contraction indices [47]. Knee braces were effective in lowering the **co**-contraction indices in patients with KOA [6]. Three studies showed that, during challenged gait (perturbations by a moveable platform) higher **co**-contraction indices in the study

Table 2

Objective parameters for knee joint stability during comfortable gait. (-) indicates that there was no data presented in the studies to calculate the difference between the groups.

Objective parameters for knee joint stability during comfortable gait			
Kinematics	Study	Conditions	Main results
1. Knee flexion angle (25% of all studies) PK: Peak flexion angle FAH: Flexion angle at heel strike FE: Flexion excursion FMS: Flexion angle at mid-stance	Alkjaer et al. 2003	ACL-I vs. ACL-S vs. Control	Higher PK during stance in ACL-S vs. control (5.9°).
	Beard et al. 1996	ACL vs. Control Injured vs. uninjured leg	No difference in PK during stance and swing. No difference in FAH. Higher FMS in ACL injured leg vs. uninjured leg (4.6°) and control (7.5°).
	Chmielewski et al. 2001	ACL-S vs. Control Injured leg vs. Uninjured leg	Lower PK during stance in ACL-S injured leg vs. uninjured leg (2.8°) and Control (5.7°).
	Gardinier et al. 2012	ACL-I, injured vs. uninjured leg	Lower PK during stance in injured leg (2.6°).
	Hurd and Snyder-Mackler 2007	ACL-I, injured vs. uninjured leg	Lower PK in injured leg during weight acceptance (-). Lower FE in injured leg during mid-stance and weight acceptance (-). No difference in FAH.
	Lewek et al. 2002	ACL vs. Control ACLR-weak vs. ACLR-strong vs. ACL-I	Lower PK during stance in ACLR-weak vs. control (5.5°). No difference in FAH.
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg	Lower PK during stance in ACL-I injured leg vs. Control (4.6°) and ACL-S (˜1.75°). Lower PK during stance in ACL -I Injured vs. uninjured leg (4°).
	Farrokhi et al 2015	KOA-I vs. KOA-S	Higher FE in KOA-I (3.5°) during early stance.
	Gustafson et al. 2016 (same dataset as farrokhi et al. 2015)	KOA-I vs. KOA-S	No difference in PK during weight acceptance. Lower FAH in KOA-I (2.3°). Higher FE in KOA-I during weight acceptance (3.3°).
	Lewek et al. 2006	KOA vs. Control Injured vs. uninjured leg	Lower FE during weight acceptance in injured leg KOA vs. uninjured leg KOA (5.8°) and control (5.1°).
	Mari et al. 2014	Cerebellar Ataxia vs. Control	No difference in FE.
	Hooper et al. 2002	Chronic posterior instability vs. Control	No difference in FE during mid-stance. No difference in FAH. No difference in flexion angle during toe off.
2. Maximal finite-time Lyapunov (18% of all studies)	Kurz et al. 2010	Parkinson vs. Control vs. Young subjects	Higher Lyapunov exponents in Parkinson vs. Control (0.23) and Young subjects (0.61). Lower Lyapunov exponents in Young subjects vs. Control (0.30).
	Myers et al. 2009	Periphal Arterial (PA) vs. Control	Higher Lyapunov exponents in PA (0.02).
	Buzzi et al. 2003	Young healthy subjects vs. elderly healthy subjects	Higher Lyapunov exponents in elderly healthy subjects (0.02).
	Decker et al. 2012	Healthy subjects With vs. without safety harness	No difference in Lyapunov exponents in the knees.
	Wu et al. 2016	Young healthy subjects Two arm swing conditions	No difference in local divergence component (Lyapunov) of the knee between the two arm swing conditions.
3. Tibiofemoral a-p translation (7% of all studies) a-p = anterior- posterior MT: mean translation RT: range of translation MAT: max translation	Boeth et al. 2013	ACL vs. Control Injured vs. uninjured leg	Lower MT in ACL injured leg vs. ACL uninjured leg (2 mm). Lower RT in ACL injured vs. ACLl uninjured leg (2.7 mm) and control (-).
	Kvist et al. 2004	ACL-Well vs. ACL-Poor Injured vs. uninjured leg	Lower MAT difference between injured leg and uninjured leg in ACL-Poor vs. ACL-Well (2.3 mm).
	Matic et al. 2016	ACL pre-surgery vs. ACL post-surgery	Lower MT in ACL post-surgery (3 mm).
	Obuchi et al. 1999	Healthy left leg vs. Healthy right leg	No difference in MT. No difference in MAT.
	Tagesson et al. 2013	Healthy boys vs. healthy girls vs. healthy men vs. healthy women	Higher MAT in women vs. men (2.1 mm).
4. Varus – valgus movement (6% of all studies) MV: Maximum varus angle MVVV: Maximum varus – valgus velocity VVE: Varus – valgus excursion	Chang et al. 2013	KOA (varus thrust) vs. KOA	Higher MV during all phases of gait except terminal stance in KOA (varus thrust) (˜0.6°). Higher MVVV in KOA (varus thrust) (6.8°/s). All values were adjusted for age, gender, BMI, gait speed and alignment.
	Sharma et al. 2015	KOA-I vs. KOA-S	No difference in VVE. No difference in MVVV.
	Skou et al. 2014	KOA	Associations between knee confidence and worse self-reported knee instability, higher pain, lower muscle strength and higher dynamic varus-valgus motion (during 20% – 80% stance phase).
	Van der Esch et al. 2008	KOA left and right leg	Varus- valgus motion is independent on joint laxity, muscle strength, skeletal alignment and joint proprioception.
5. Relative phase dynamics (4% of all studies)	Kurz et al. 2005	ACL vs. Control	Lower mean relative phase in ACL (7.6°).
	Hutin et al. 2011	Hemiparetic vs. Control Hemiparetic, pre vs. post botox Control, free vs. constrained	Lower root mean square relative phase in control constrained during full gait cycle. (˜27). Higher relative phase reversals in Hemiparetic pre-botox during full gait cycle vs. Control free (4.7) and Control constrained (2.9).

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Table 2 (*continued*)

Objective parameters for knee joint stability during comfortable gait

Kinematics	Study	Conditions	Main results
6. 3D knee angles (4% of all studies)	Jones et al. 1983	ACL-I vs. control	The measurement of knee angles with the triaxial electrogoniometer system was not able to provide enough information to classify knee instability during walking (-).
7. Maximum Floquet multiplier (3% of all studies)	Dingwell et al. 2007	Neuropathy vs. Control vs. Young healthy control	Lower maximum Floquet multiplier in Neuropathy compared to controls(-).
	Hurmuzlu et al. 1996	Post-polio vs. Control Post-polio grouped by hip flexor strength	Higher maximum Floquet multiplier in Post-polio (0.2). Higher maximum Floquet multiplier in Post-polio with weak hip flexor compared to control (0.3) and strong hip flexor (0.2).
8. Tibial rotation (3% of all studies)	Bohn et al. 2015	Comparison ACL surgery	No difference in maximal tibial rotation between surgery techniques.
	Claes et al. 2011	ACL vs. Control Comparison ACL surgery	No difference in tibial rotation excursion between ACL and Control. No difference in tibial rotation excursion between surgery techniques.
	Matic et al. 2016	ACL, pre-surgery vs. post-surgery	Lower mean tibial rotation post-surgery (3.1°).
9. Knee accelerations (3% of all studies)	Turcot et al. 2009	KOA vs. Control Pre- vs. Post treatment	Higher range of anterior-posterior accelerations in KOA (1 g). Lower anterior-posterior accelerations after treatment in KOA (0.12 g).
	Khan et al 2013	Arthroplasty vs. Control	No difference in mean anterior-posterior acceleration.
	Roberts et al. 2013	Arthroplasty vs. Control	Higher range of anterior-posterior accelerations in arthroplasty (0.3 g). Higher range of superior-inferior accelerations in arthroplasty (0.2 g).
12. Nyquist and Bode criteria (1% of all studies)	Morgan et al. 2016	ACL vs. Control Injured vs. uninjured leg	Lower phase margins in ACL injured leg compared to control during initial contact (44.5°). Higher phase margins in ACL uninjured compared to control during 15% of stance (51.1°) and 30% of stance (46.2°).
Kinetics	*Study*	*Conditions*	*Main results*
15.Knee flexion – extension moment (15% of all studies) PE: Peak Extensor moment PF: Peak Flexion moment EI: Extensor moment at initial knee extension	Alkjaer et al. 2003	ACL-I vs. ACL-S vs. Control	No difference in PE between groups.
	Chmielewski et al. 2001	ACL vs. Control Injured leg vs. Uninjured leg	No difference in PE.
	Gardinier et al. 2012	ACL-I, injured vs. uninjured leg	Lower PE in injured leg during (0.1 Nm/kg*m).
	Hurd and Snyder-Mackler 2007	ACL-I injured vs. uninjured leg	Lower PF in injured leg (-). Lower PE in injured leg (-).
	Lewek et al. 2002	ACL vs. Control ACLR-weak vs. ACLR-strong vs. ACL-I	Lower PF in ACLR-weak (0.5 %BW*LL) and ACL-I (0.3 %BW*LL)) compared to Control.
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg	Lower PE in ACL-I injured leg (˜0.2 N*m/kg).
	Farrokhi et al. 2015	KOA-I vs. KOA-S	Higher EI in KOA-I (6.4 Nm/kg). No difference in moment at early stance.
	Gustafson et al. 2016	KOA-I vs. KOA-S	No difference in PE or PF.
	Lewek et al. 2006	KOA vs. Control Injured vs. uninjured leg	Lower PE in injured leg KOA vs. uninjured leg KOA (0.16 Nmm/kgm) and controls (0.12 Nmm/kgm).
	Hooper et al. 2002	Posterior stability vs. Control	No difference in PE or PF.
16. Ground reaction forces (6% of all studies)	Chmielewski et al. 2001	ACL-S vs. Control Injured leg vs. Uninjured leg	Lower force during loading response in ACL-S injured leg vs. control (0.09 N).
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg	Lower force during loading response in both ACL groups (both legs) vs. control (˜6.5%BW).
17. Total support moment (4% of all studies)	Chmielewski et al. 2001	ACL-S vs. Control Injured leg vs. Uninjured leg	Higher total support moment in ACL-S injured leg vs.ACL-s uninjured leg (0.17 Nm/kg).
	Hurd and Snyder-Mackler 2007	ACL-I injured vs. uninjured leg	Lower contribution of the knee to the total support moment injured leg during weight acceptance(-).
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg	Lower contribution of the knee to the total support moment in ACL-I during weight acceptance (-).
	Farrokhi et al 2015	KOA-I vs. KOA-S	Lower total support moment in KOA-I during early stance (6.5 Nm/kg).
Electromyography	*Study*	*Conditions*	*Main results*
19. Amplitude of muscle activation (18% of all studies) RMS: Root Mean Square ARV: Average rectified Value IL: Integral VM: Vastus medialis VL: Vastus Lateralis BF: Biceps Femoris MH: Medial Hamstrings SOL: Soleus MG: Medial Gastrocnemius LH: Lateral Hamstrings TA: Tibialis Anterior LG: Lateral Gastrocnemius RF: Rectus Femoris	Alkjaer et al. 2003	ACL-I vs. ACL-S vs. Control VM, VL, BF, MH	No difference in mean amplitude of muscle activation between groups.
	Chmielewski et al. 2002	ACL Pre- vs. Post training SOL, MG, VL, LH	Higher IL VL activation in ACL after (post) perturbation training (-).
	Hurd and Snyder-Mackler 2007	ACL-I injured vs. uninjured leg VL, VM, TA, MG, LG, SOL, MH, LH	Higher LH ARV (2.4) and MH (1.3) in injured leg during midstance. Lower SOL ARV in injured leg during midstance (5.1). Lower VL ARV (6.7) and VM (7.6) in injured leg during weight acceptance. Higher LH ARV in injured leg during weight acceptance (2.8).
	Lewek et al. 2002	ACL vs. Control ACLR-weak vs. ACLR-strong vs. ACLD MG, VL, LH	No differences in IL of MG, VL, LH.

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Table 2 (*continued*)

Objective parameters for knee joint stability during comfortable gait

Kinematics	Study	Conditions	Main results
SM: Semimembranosis SA: Sartorius GR: Gracilis TFL: Tensor Fascia Latae GM: Gluteus maximus	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg MG, SOL, VL, LH	Higher IL SOL during weight acceptance in ACL-I injured leg (˜2.1).
	Fantini Pagani et al. 2013	KOA No brace vs. 4° Valgus brace vs. Neutral flexible brace RF,VL,VM, LG, MG	Lower RF RMS in neutral flexible brace during pre-activation compared to no brace (8%). Lower RF RMS in both brace conditions during late stance (˜5%). Lower LH RMS in both brace conditions during late stance (˜3.6%). Lower LG RMS in 4° valgus brace during loading response compared to no brace (9.2%). Lower LG RMS in both brace conditions during early stance (˜7.4).
	Hortobagyi et al. 2005	KOA vs. Control vs. Young adults VL, BF	No differences in amplitude of muscle activation.
	Sharma et al. 2017	KOA VM, VL, SM, BF	Higher SM & BF activation during late stance and early swing compared to reported muscle activation patterns in healthy subjects (-).
	Mari et al. 2014	Cerebellar Ataxia vs. Control VL, MG, BF, TA	Higher VL, BF, TA activation in Cerebellar Ataxia patients (-).
	Sturnieks et al. 2011	Arthroscopic partial meniscectomy (APM) weak vs. APM Normal vs. Control VM, VL, RF, SM, BF, MG, LG, SA, GR, TFL	Higher BF and SM activation in both APM groups from initial contact till midstance (-). Higher VM, VL, RF activation in both APM groups during midstance.
	Yamashita et al. 1999	Healthy infants TA, LG, VM, RF, BF, GM	Activity of the LG and VM during late swing can be an indicator of stability at the stage of walking development (-).
20. Co-contraction index (10% of all studies) VLLH: Vastus Lateralis & Lateral Hamstrings VLSM: Vastus Lateralis & Semimembranosis VMMG: Vastus Medialis & Medial Gastrocnemius VMMH: Vastus Medialis & Medial Hamstrings RFVMMGMH: Rectus Femoris, Vastus Medialis, Medial Gastrocnemius and Medial Hamstring	Hurd and Snyder-Mackler 2007	ACL-I injured vs. uninjured leg	Higher VLLH co-contraction index in injured leg during mid-stance (-).
	Collins et al. 2014	KOA vs. Control Injured vs. uninjured leg	No differences in VLSM index.
	Lewek et al. 2006	KOA vs. Control Injured vs. uninjured leg	Higher VLLH co-contraction index in KOA injured leg vs. KOA uninjured leg (8.2). Higher VMMG co-contraction index in KOA both legs (˜5.9).
	Ramsey et al. 2007	KOA No brace vs. neutral brace vs. valgus brace	Lower VMMH co-contraction index in valgus brace vs. no brace (-). Lower VLLH co-contraction index in neutral brace and valgus brace vs. no brace (-).
	Centomo et al. 2007	Trans-tibial amputee leg vs. intact leg vs. Control	Lower RFVMMGMH index during single limb support in transtibial amputee leg vs. control (30.8%). Lower RFVMMGMH index during single limb support in intact leg vs. control (17.9%).
21. Co-contraction ratio (7% of all studies) VLLG: Vastus Lateralis & Lateral Gastocnemius VMSM: Vastus Medialis & Semimembranosis HQ: Hamstrings & Quadriceps VLBF: Vastus Lateralis & Biceps Femoris	Fantini Pagani et al. 2013	KOA No brace vs. 4° Valgus brace vs. Neutral flexible brace	Lower flexor-extensor co-contraction ratio in 4° valgus brace during loading phase (15.1%) and late stance (21.5%) compared to no brace. Lower VLLG co-contraction ratio in 4° valgus brace during loading phase (28.4%) compared to no brace. Lower VLLH co-contraction ratio in 4° valgus brace(5.9%) and neutral flexible brace (16.8%) during pre-activation phase. Lower VMMH co-contraction ratio in in 4° valgus brace(10.4%) and neutral flexible brace (19.6%) during pre-activation phase.
	Sharma et al. 2017	KOA	Higher VMSM co-contraction ratio compared to VLBF co-activity ratio.
	Sturnieks et al. 2011	Arthroscopic partial meniscectomy (APM) weak vs. APM Normal vs. Control	No difference in HQ co-contraction ratio.
	da Fonseca et al. 2006	Healthy subjects Men vs. Women Athletic vs. Sedentary	Higher VLBF co-contraction ratio in sedentary women compared to athletic women (2.5 % MVC).
22.Muscle onset time (6% of all studies)	Chmielewski et al. 2002	ACL Pre- vs. Post training SOL, MG, VL, LH	No difference in muscle onset time.
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg MG, SOL, VL, LH	Earlier MG onset time in ACL-I injured leg (-).
23. Duration of muscle activation (3% of all studies) Q: Quadriceps H: Hamstrings G: Gastrocnemius	Beard et al. 1996	ACL vs. Control Injured vs. uninjured leg Q, H, G	Longer H duration in ACL injured leg vs. control (15.6%).
	Rudolph et al. 2001	ACL-I vs. ACL-S vs. Control Injured vs. uninjured leg MG, SOL, VL, LH	Longer MG and LH duration in ACL -I (-).

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Table 2 (*continued*)

Objective parameters for knee joint stability during comfortable gait

Kinematics	Study	Conditions	Main results
24. Co-activation index (3% of all studies) TAMG: Tibialis Anterior & Medial Gastrocnemius RFBF: Rectus Femoris & Biceps Femoris	Alkjaer et al. 2003	ACL-I vs. ACL-S vs. Control VLBF	No difference in VLBF co-activation index.
	Mari et al. 2014	Cerebellar Ataxia (CA) vs. Control	Higher VLBF co-activation index in CA during double support, single support and swing phase (˜4.4). Higher TAMG co-activation index in CA during whole gait cycle (5.6).
	Boudarham et al. 2016	Multiple Sclerosis (MS) vs. Control Injured vs. uninjured leg	Lower RFBF & VLBF index during initial double support phase in MS (-). Higher RFBF & VLBF index during single support phase in MS (-) No difference between injured and uninjured leg.
25. Co-activation ratio (3% of all studies)	Hortobagyi et al. 2005	KOA vs. Control vs. Young healthy subjects	No differences in VLBF ratio.
	Sharma et al. 2017	KOA	Lower VLBF co-activity ratio compared to VMSM co-contraction ratio.
27. Co-activation duration (1% of all studies) TASOL: Tibialis Anterior & Soleus	Boudarham et al. 2016	Multiple Sclerosis (MS) vs. Control Injured vs. uninjured leg	Longer RFBF & VLBF activation duration during single support phase in MS (-). Shorter TASOL activation duration during final double support phase in MS (-). No difference between injured and uninjured leg.
29. Principal Component Analysis (1% of all studies)	Hubley-Kozey et al. 2006	KOA vs. Control RF, VL, VM, LH, SM, LG, MG	83% of the variance of the wavevorm could be explained by the PP in both groups; similar muscle activations in both groups. PP scores differed which indicate small changes in neuromuscular control which might be caused by changes in mechanical environment of the joint (instability).
Combination	*Study*	*Conditions*	*Main results*
31. Knee joint stiffness (6% of all studies)	Collins et al. 2014	KOA vs. Control Injured vs. uninjured leg	No difference in knee joint stiffness.
	Gustafson et al. 2016	KOA-I vs. KOA-S	Higher knee joint stiffness in KOA-S (0.2 % BW*HT/°).
	Galli et al. 2017	Cerebral palsy (CP) vs. control	No difference in knee joint stiffness.
32. Variability index (2% of all studies)	Lewek et al. 2006	KOA vs. Control Injured vs. uninjured leg	Higher frontal plane index in KOA uninjured leg. No difference in sagittal plane index.
33.Modeling muscle forces (2% of all studies)	Gardinier et al. 2012	ACL-I, injured vs. uninjured leg	Lower extensor muscle force in injured leg (0.53 BW). Lower flexor muscle force in injured leg (0.23 BW).

group during or after the perturbation compared to controls [11,50,80]. Perturbation training was effective in lowering these **co**-contraction indices both during, and after perturbation in patients with ACL-S [50]. Apps et al. [37] reported higher **co**-contraction indices in healthy subjects when wearing instability shoes.

3.9. Co-contraction ratio

This measure was quite similar to the **co**-contraction index, but the result of the calculation was expressed in percentages. The **co**-contraction ratio was used in 6% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2, 4 studies) and challenged gait (Table 3,2 studies). The studies investigated patients with KOA, an ACLinjury, Arthroscopic partial meniscectomy (APM) patients and healthy subjects. During comfortable gait higher **co**-contraction ratios were present in the muscles of the medial side of the knee compared to the lateral side of patients with KOA [94]. Da Fonseca et al. [53] showed that healthy women with sedentary behavior had a higher **co**-contraction ratio compared to athletic women. No difference was observed in the **co**-contraction ratios of patients with APM compared to control subjects [97]. Knee braces were able to lower the **co**-contraction ratios in patients with KOA [59]. During challenged gait, lower **co**-contraction ratios were observed pre- and post-perturbation in patients with an ACL injury compared to control [30]. Statsny et al. [96] showed lower **co**-contraction ratios between different types of load-carrying walking.

3.10. Muscle onset time

Patients with knee joint instability are presumed to have altered neuromuscular activity and therefore also have altered muscle onset time. Muscle onset time was used in 6% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2,2 studies) and challenged gait (Table 3,3 studies). The populations investigated with electromyography were patients with an ACL injury and healthy male subjects. During comfortable gait, earlier medial gastrocnemius onset time was observed in the injured leg of patients with ACL-I compared to control [88]. Chmielewski et al. [49] showed no difference in muscle onset time after perturbation training in patients with an ACL injury. During challenged gait, altered muscle onset times were reported in the study group during uphill walking (compared to control) [70,95] and during load-carrying gait (between different load conditions) [96].

3.11. Knee joint stiffness

Patients with knee joint instability are expected to stiffen their knee joint as a compensation method for their lack of stability. Knee joint stiffness was used in 6% of all studies as objective parameter for knee joint stability, during comfortable gait (Table 2,3 studies) and challenged gait (Table 3,2 studies). The studies investigated patients with KOA, Cerebral Palsy (CP) or healthy subjects. Knee joint stiffness was calculated by dividing the knee extensor moment by the knee flexion angle. During comfortable gait, one study reported higher knee joint stiffness in patients with KOA compared to the control group [20], but a different study with patients with KOA did not observe this difference [52]. Likewise, a study with children with CP also did not report a difference in knee joint stiffness compared to control subjects [60]. During challenged gait, a higher stiffness was observed in patients with severe knee osteoarthritis at three gait speeds compared to patients with mild knee osteoarthritis and a control group [33]. An instability shoe lowered the knee joint stiffness in healthy females [37].

Table 3
Objective parameters for knee joint stability during challenged gait. (-) indicates that there was no data presented in the studies to calculate the difference between the groups.

Objective parameters for knee joint stability during challenged gait			
Kinematics	Study	Conditions	Main results
1. Knee flexion angle (25% of all studies) PK: Peak flexion angle FE: Flexion excursion FAH: Flexion angle at heel strike FMS: Flexion angle at mid-stance FT: Flexion angle during terminal stance phase	Chmielewski et al. 2005	ACL-S vs. Control Pre-training vs. Post-training Level (L) vs. Perturbed Lateral(PL) vs. Perturbed Anterior (PA)	Lower PK during stance in ACL-S pre-training (5°). No difference in FE. Higher PK during stance standard deviation in ACL-S (PL) post training (0.9°).
	Fuentes et al. 2011	ACL-I vs. Control Comfortable gait speed vs. fast gait speed (+20%)	Higher FT in ACL-I at comfortable gait speed (3.8°). No difference at fast gait speed.
	Rudolph et al. 1998	ACL-I vs. ACL-S Injured vs. uninjured leg Walkway with obstacles	Lower FAH in injured leg ACL-I (-).
	Tibone et al. 1986	ACL-I Injured vs. uninjured leg Comfortable gait speed vs. fast gait speed (-)	No difference in knee flexion angle during both gait speeds (-).
	Yim et al. 2014	ACL Injured vs. uninjured leg Controlled comfortable gait speed vs. fast gait speed (+20%)	Higher FAH in injured leg at both speeds (-). Higher FMS in injured leg at both speeds (-).
	Farrokhi et al. 2012	KOA-I vs. control KOA-I medial vs. KOA-I medial + lateral Downhill walking (7% grade)	Lower FE in KOA-I during loading response (˜8°), independent of KOA location. No difference in FAH.
	Farrokhi et al. 2014	KOA-I vs. KOA-S vs. Control Downhill walking (7% grade)	No difference in FAH. No difference in FE during loading response.
	Kumar et al. 2013	KOA vs. Control Level (L) vs. Perturbed (P)	Lower FE in KOA during loading response (both L & P) (˜4°). Higher FAH in KOA (both L & P) (˜3°). Similar responses in flexion angle in both groups on perturbations.
	Apps et al. 2016	Healthy females 3 shoe conditions: Unstable (US) vs. Irregular midsole (IM) vs. Control	Lower FE during loading response in IM vs. US (3.1°) and control (1.7°). Lower FE during loading response in US vs. control (1.4°). Higher FE during propulsion in IM vs. US (3.3°) and control (4.1°).
	Horsak and Baca 2013	Healthy subjects Instability shoe vs. Control shoe	Lower FE in instability shoes (2.5°). Lower PK during swing in instability shoes (2.6 °). No difference in PK during loading response.
2. Maximal finite-time Lyapunov (18% of all studies)	Stergiou et al. 2004	ACL, injured vs. uninjured leg Slow (-20%) vs. normal vs. fast gait speed (+20%)	Higher Lyapunov exponents in ACL injured leg (˜0.0065). No differences between gait speed.
	Fallah-Yakhdani et al. 2010	KOA vs. Control Injured vs. uninjured leg Pre- vs. post-surgery Gait speed (0.6 – 5.4 km/h, increments of 0.8 km/h)	Higher short term Lyapunov in KOA uninjured leg pre-surgery compared to control (-). Lower long term Lyapunov in KOA injured leg pre-surgery compared to control (-). No difference post-surgery (-). Lower short term lyapunov and higher long term lypanov with increasing walking speed in both groups (-).
	Fallah-Yakhdani et al. 2012 (follow up analysis with same data as above)	KOA vs. Control Injured vs. uninjured leg Pre- vs. post-surgery Gait speed (0.6 – 5.4 km/h, increments of 0.8 km/h)	Lyapunov exponents in KOA pre-surgery are a predictor for co-contraction time.
	Mahmoudian et al. 2016 (follow up analysis with same data as above)	KOA vs. Control vs. Young healthy subjects Gait speed (1.4 – 5.4 km/h)	Lower local divergence component (Lyapunov) in KOA around 40-70% of gait cycle compared to young healthy subjects (-).
	Segal et al. 2010	Transtibial amputees vs. intact knee Straight line gait vs. turning gait	No differences in Lyapunov exponents (for both types of gait).
	Bulea et al. 2017	Cerebral Palsy (CP) vs. Control Unloaded vs. loaded Dominant leg vs. non-dominant leg	Higher Lyapunov exponents in CP dominant leg vs.CP non-dominant leg (0.13). Higher Lyapunov exponents in loaded condition in CP (-).
	Manor et al. 2008	Periphal neuropathy vs. Control Three gait speeds (60%, 80% & 100%)	No differences in short and long term Lyapunov exponents between groups. Higher short and long term Lyapunov exponents in 100% gait speed.
	Beaudette et al. 2015	Healthy subjects Unloaded vs. Load at thigh or shank or foot	Higher Lyapunov exponents in load on thigh condition (˜0.067).
	Russell et al.2014	Healthy subjects Controlled gait speed vs. free gait speed 7 stride frequencies (± 5, ± 10, ± 15 strides / min)	Higher Lyapunov exponents for higher or lower stride frequencies than the preferred stride frequency at both speeds (-). Higher Lyapunov exponents for controlled gait speed for non-preferred stride frequencies (-).

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Table 3 (*continued*)

Objective parameters for knee joint stability during challenged gait

Kinematics	Study	Conditions	Main results
	Russell et al. 2016	Healthy subjects No load vs. Symmetrical load vs. asymmetrical load Controlled gait speed (+ controlled stride frequency) vs. free gait speed (+ free stride frequency)	Higher Lyapunov exponents for both the symmetrical load and the asymmetrical load (-). Higher Lyapunov exponents in symmetrical load compared to asymmetrical load (-). No difference in gait speeds.
	Segal et al. 2008	Healthy subjects, right and left knee Two gait speeds (0.95 and 1.2 m/s) Straight line gait vs. turning gait	Higher Lyapunov exponents in right knee during turning gait at both gait speeds (0.14 for 0.95 m/s and 0.16 for 1.2 m/s).
3. Tibiofemoral a-p translation (7% of all studies)	Yim et al. 2014	ACL, injured vs. uninjured leg Comfortable gait speed vs. fast gait speed (+20%)	Lower mean translation (MT) in ACL-injured (-). No difference between gait speeds.
4. Varus – valgus movement (6% of all studies)	Farrokhi et al. 2016	KOA vs. Control Downhill walking (7% grade)	Higher varus excursion (VE) in KOA (0.8°). No difference in maximum varus angle (MV). No difference in varus – valgus angle at heel strike.
5. Relative phase dynamics (4% of all studies) MR: Mean Relative phase DP: Deviation Phase	Donker and Beek 2002	Amputee vs. Control Amputee leg vs. uninjured leg Gait speed change (0.5 – 3.5 km/h, steps of 0.5 km/h)	Lower MR in amputee leg and uninjured leg vs. between the legs of the controls (4.1). Difference between groups decreased with increasing gait speed (-).
	Lu et al. 2008	Healthy young subjects Leading limb vs. trailing limb Walkway with obstacles	Higher Knee-Ankle DP value in leading limb during stance phase (˜15.5°). Lower Knee-Ankle DP value in leading limb during swing phase (˜24.5°). Higher Knee-Ankle DP value with increasing obstacle height (-). Lower Hip-Knee DP value in leading limb during swing phase (˜11.8°).
6. 3D knee angles (4% of all studies) AB-AD: abduction-adduction angle IN-EX: internal-external rotation angle	Farrokhi et al. 2012	KOA-I vs. control KOA-I medial vs. KOA-I medial + lateral Downhill walking (7% grade)	Higher AD excursion during loading response in KOA-I medial (1.2°). Higher AB excursion during loading response in KOA-I medial + lateral (2.9°). Higher AB at initial contact in KOA-I medial + lateral vs. control (4.6°) and KOA-I medial (6.6°). Lower IN excursion during loading response in both KOA-I groups (˜3.5°). Higher IN at initial contact in KOA-I medial + lateral vs. control (8.4°) and KOA-I medial (8.8°).
	Farrokhi et al. 2014	KOA-I vs. KOA-S vs. Control Downhill walking (7% grade)	Higher adduction contact point excursion in KOA vs. control (˜1°). Lower extension – flexion angular velocity during heel strike in KOA-I (93.6°/s). Lower mean knee extension – flexion angular velocity in KOA-I vs. control (44.2°/s). Lower adduction angular velocity during heel strike in KOA-S (˜23.2 °/s). Lower peak adduction angular velocity in KOA-S vs. Control (˜25.3 °/s).
	Yim et al. 2014	ACL Injured vs. uninjured leg Comfortable gait speed vs. fast gait speed (+20%)	No difference in AB-AD angle at both speeds. No difference in IN-EX at both speeds.
7. Maximum Floquet multiplier (3% of all studies)	Arellano et al. 2009	Healthy subjects Load-carrying walking (0, 10, 20 & 30% BM)	No difference in maximum Floquet multiplier between weight conditions.
10. Knee contact point movement (2% of all studies)	Farrokhi et al. 2014	KOA-I vs. KOA-S vs. Control Downhill walking (7% grade)	Higher total length of medial compartment contact path in KOA-I (˜4 mm). Higher mean medial compartment contact point velocity in KOA-I (31.9 mm/s).
	Farrokhi et al. 2016	KOA vs. Control Downhill walking (7% grade)	Higher medial-lateral contact point excursion in medial and lateral compartment in KOA (˜1.2 mm). Higher contact point velocity in medial and lateral compartment in KOA at heel strike(˜28.7 mm /s). Higher peak medial-lateral contact point velocity in the medial compartment of KOA (17.2 mm/s).
11. 3D knee translations (1% of all studies)	Farrokhi et al. 2012	KOA-I vs. control KOA-I medial vs. KOA-I medial + lateral Downhill walking (7% grade)	No difference in lateral or anterior translations.
13 Perturbation Recovery time (1% of all studies)	Li et al. 2005	Young healthy females Gait speed (0.67 – 1.34 m/s)	Mean time for the knee flexion angle to recover to steady state after perturbation was 1.2 ± 0.6 s. Gait speed did not change recovery time.
14. Gait sensitivity norm (1% of all studies)	Van den Noort et al. 2017	Healthy subjects Level walking vs. perturbed walking	The gait sensitivity norm parameters were shown to be feasible in quantifying the responses of certain gait parameters during perturbed gait (-).

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Table 3 (*continued*)

Objective parameters for knee joint stability during challenged gait

Kinematics	Study	Conditions	Main results
Kinetics	*Study*	*Conditions*	*Main results*
15.Knee flexion – extension moment (15% of all studies) PF: Peak Flexion moment PE: Peak Extensor moment	Rudolph et al. 1998	ACL-I vs. ACL-S Injured vs. uninjured leg Walkway with obstacles	Lower PF in injured leg of ACL-I and ACL-S (-). No difference in PE.
	Apps et al. 2016	Healthy females 3 shoe conditions: Unstable (US) vs. Irregular midsole (IM) vs. Control	No differences in PE and PF between shoe conditions (-).
	Horsak and Baca 2013	Healthy subjects Instability shoe vs. Control shoe	No difference in knee flexion-extension moment between shoes (-).
16. Ground reaction forces (6% of all studies)	Rudolph et al. 1998	ACL-I vs. ACL-S Injured vs. uninjured leg Walkway with obstacles	Lower peak force in injured leg in both groups (-).
	Tibone et al. 1986	ACL-I Injured vs. uninjured leg Comfortable gait speed vs. fast gait speed (-)	No differences in forces at both speeds.
	Horsak and Baca 2013	Healthy subjects Instability shoe vs. Control shoe	Higher first peak force during walking with instability shoe (4.6%BW).
18. Knee rotational moment (1% of all studies)	Fuentes et al. 2011	ACL-I vs. Control Comfortable gait speed vs. fast gait speed (+20%)	Lower maximum knee rotational moment in ACLD during terminal phase of gait at comfortable gait speed (0.15 % BW*Ht) and at fast gait speed (0.2%BW*Ht).
Electromyography	*Study*	*Conditions*	*Main results*
19. Amplitude of muscle activation (18% of all studies) RMS: Root Mean Square VM: Vastus medialis VL: Vastus Lateralis MH: Medial Hamstrings LH: Lateral Hamstrings MG: Medial Gastrocnemius BF: Biceps Femoris MQ: Medial Quadriceps LQ: Lateral Quadriceps LG: Lateral Gastrocnemius TA: Tibialis Anterior GM: Gluteus maximus PL: Peroneus Longus	Sinkjaer et al. 1991	ACL-I vs. ACL-S vs. Control Level vs. uphill walking (2.25°- 11.25°) VM, VL, MH, LH, MG	Higher MG RMS in ACL with increasing in incline (-). Higher MG RMS in ACL-S compared to ACL-I with increasing incline (-).
	Tibone et al. 1986	ACL-I Injured vs. uninjured leg Comfortable gait speed vs. fast gait speed (-) VM, MH, BF, MG	No differences in amplitude of muscle activation.
	Kumar et al. 2013	KOA vs. Control Level (L) vs. Perturbed (P) MQ, LQ, MH, LH, MG, LG	Higher LH activation in KOA during loading response (both L & P) (˜10%). Similar responses in amplitudes of muscle activation in both groups on perturbations.
	Apps et al. 2016	Healthy females 3 shoe conditions: Unstable (US) vs. Irregular midsole (IM) vs. Control MG, TA	Higher MG activation during pre-activation in IM vs. US (10.3%) and control (9.8%). Higher MG activation during loading response in IM vs. US (5.8%) and control (7.2%). Lower TA activation during pre-activation in IM vs. US (17.5%) and control (15,6%).
	Horsak and Baca 2013	Healthy subjects Instability shoe vs. Control shoe GM, VM, VL, BF, TA, PL, MG	Higher VM and VL activation in instability shoe during late stance.
20. Co-contraction index (10% of all studies) VLLH: Vastus Lateralis & Lateral Hamstrings VLMG: Vastus Lateralis & Medial Gastrocnemius VLBF: Vastus Lateralis & Biceps Femoris MQH: Medial Quadriceps & medial Hamstrings MQG: Medial Quadriceps & medial Gastrocnemius MGTA: Medial Gastrocnemius & Tibialis Anterior	Chmielewski et al. 2005	ACL-S vs. Control Pre- vs. post-training Level (L) vs. Perturbed Lateral(PL) vs. Perturbed Anterior (PA)	Higher VLLH index in ACL-S (L) pre-training during preparatory phase (8.4) and weight acceptance phase (11.3). Higher VLLH index in ACL-S (PL) pre-training during preparatory phase (7.8) and weight acceptance phase (17.3). Higher VLLH index in ACL-S (PA) pre-training during weight acceptance phase (11.75). Higher VLMG index in ACL-S (PL) (5.2) & (PA) (4.4) pre-training during preparatory phase. Lower VLLH index within ACL-S (PL) post-training during preparatory phase (7.9) and weight acceptance phase (9.4). Lower VLLH index within ACL-S (PA) post-training during preparatory phase (6.3) and weight acceptance phase (11.8). Lower VLMG index within ACL-S (PA) post-training during weight acceptance phase (7.1).
	Lustosa et al. 2011	ACL Full return group vs. limited return group Injured vs. uninjured leg Pre- vs. post perturbation	Lower VLBF index in injured leg full return group pre-perturbation compared to uninjured leg (0.01). Lower VLBF index in injured leg limited return group pre-perturbation compared to uninjured leg (0.003). Higher VLBF index in limited return group post perturbation in both legs compared to full-return group (˜0.02).
	Schmitt and Rudolph 2008	KOA-I vs. KOA-S Perturbations	Higher MQH index in KOA-I during preparation and weight acceptance (-). Higher MQG index in KOA-I during weight acceptance (-).
	Apps et al. 2016	Healthy females 3 types of shoes: Unstable (US) vs. Irregular midsole (IM) vs. control	Higher MGTA index during pre-activation in IM vs. US (10.8) and control (11.7). Higher MGTA index during loading response in IM vs. US (2.7) and control (3.8). Higher MGTA index during propulsion in IM vs. US (1.8).

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Table 3 (*continued*)

Objective parameters for knee joint stability during challenged gait

Kinematics	Study	Conditions	Main results
21. Co-contraction ratio (7% of all studies) VLBF: Vastus Lateralis & Biceps Femoris VMVL: Vastus Medialis & Vastus Lateralis	da Fonseca et al. 2004	ACL vs. Control Injured vs. uninjured leg Pre- vs. post perturbation	Lower VLBF ratio in ACL pre-perturbation and post-perturbation (-). No difference between injured and uninjured leg.
	Stastny et al. 2014	Healthy men Load-carrying walking (0, 25, 50 &75% BM)	Lower VMVL ratio in 75% BM vs. 50% BM (0.08%).
22.Muscle onset time (6% of all studies)	Kalund et al. 1990	ACL-I vs. Control Comfortable gait speed (2.5 km/h) vs. fast gait speed (4 km/h) Level vs. uphill walking (25°) VL, VM, LH, MH	No differences in muscle onset time at two walking speeds during level walking. Later LH (11.6%) and MH (11.7%) onset time in ACL-I at comfortable walking speed during uphill walking. Later LH (6.6%) and MH (11.1%) muscle onset time in ACL-I at fast walking speed during uphill walking.
	Sinkjaer et al. 1991	ACL-I vs. ACL-S vs. Control Level vs. uphill walking (2.25°- 11.25°) VM, VL, MH, LH, MG	Earlier onset times of all muscles in ACL at level walking and at all inclines (-). Earlier MG onset time in ACL-S compared to ACL-I at all inclines (-).
	Stastny et al. 2014	Healthy men Load-carrying walking (0, 25, 50 &75% BM) VM, VL, BF	Earlier VL onset time during 75% load-carrying walking compared to 50% load-carrying walking (5.8%). Later VL onset time during 0% load-carrying walking (˜7.3%).
23. Duration of muscle activation (3% of all studies)	Sinkjaer et al. 1991	ACL-I vs. ACL-S vs. Control Level vs. uphill walking (2.25°- 11.25°) VM, VL, MH, LH, MG	Longer duration in VL, VM, LH and MG muscles in ACL at level walking and at all inclines (-). Longer duration in MG muscle in ACL-S at all inclines (-).
25. Co-activation ratio (3% of all studies)	Stastny et al. 2014	Healthy men Load-carrying walking (0, 25, 50 &75% BM) VMVL	No difference in VLBF ratio between load conditions.
26. co-contraction area (2% of all studies)	Seyedali et al. 2012	Trans-tibial amputee leg vs. intact leg vs. Control Three gait speeds (self-selected (SS), +10% & -10%)	Higher VLBF co-contraction area in Trans-tibial amputee leg during early-midstance at SS compared to control (0.33). Higher VLBF co-contraction area in Trans-tibial amputee leg during late swing at SS (˜0.5).
28. Co-contraction time (1% of all studies) VMMG: Vastus Medialis & Medial Gastrocnemius VMBF: Vastus Medialis & Biceps Femoris	Fallah-Yakhdani et al. 2012	KOA vs. Control Injured vs. uninjured leg Pre- vs. post-surgery Gait speed (0.6 – 5.4 km/h, increments of 0.8 km/h)	Longer VMMG co-contraction time in KOA patients injured leg pre-surgery (-). Longer VLBF and VMBF co-contraction time in KOA patients uninjured leg pre-surgery (-).
30. Deviation index (1% of all studies)	Boerboom et al. 2001	ACL-I vs. ACL-S vs. Control Comfortable gait speed vs. fast speed, vs. slower speed (-) VM, VL, SM, BF, MG, LG	Higher deviation index of semimembranosis in ACL-S vs. ACL-I (0.4).
Combination	*Study*	*Conditions*	*Main results*
31. Knee joint stiffness (6% of all studies)	Zeni and Higginson 2009	KOA-Severe vs. KOA-Mild vs. Control Controlled comfortable gait speed (1.0 m/s) vs. self-selected gait speed vs. fastest gait speed (-)	Higher knee joint stiffness in KOA-Severe at set gait speed (˜0.03 Nm/°) and fastest gait speed (˜0.02 Nm/°). Higher knee joint stiffness in KOA-Severe at self-selected gait speed compared to control (0.02 Nm/°).
	Apps et al. 2016	Healthy females 3 types of shoes: Unstable (US) vs. Irregular midsole (IM) vs. control	Lower knee joint stiffness in US during loading phase vs. control (0.014 Nm/Kg/ °). Lower knee joint stiffness in IM during propulsion vs. US (0.8 Nm/Kg/ °) vs. CS (2.57 Nm/Kg/ °).
32. Variability index (2% of all studies)	Gustafson et al. 2015	KOA-I vs. KOA-S vs. Control Downhill walking (7% grade)	Higher sagittal plane knee kinematics variability index in KOA-I compared to Control (16.8). Lower sagittal plane knee kinematics variability index in KOA-S compared to Control (9.60) and KOA-I (26.4). Higher medial tibia anterior-posterior translation contact point variability index in KOA-I (˜21.7).
	Debbi et al. 2012	Healthy subjects Instability shoe with 3 stages of stability (0,1,2)	Higher knee flexion moment index in instability shoe 1 & 2 (˜63.1). Higher knee varus moment index in instability shoe 1 compared to instability shoe 0 (24.9). Higher knee varus moment index in instability shoe 2 compared to instability shoe 0 (36.7). Higher knee varus moment index in instability shoe 2 compared to instability shoe 1 (11.8). Higher knee flexion angle index in instability shoe 2 (˜0.65). Higher knee varus angle index in instability shoe 1 & 2 (˜1.51). Higher knee extension angle index in instability shoe 2 compared to instability shoe 0 (˜0.84).
33.Modeling muscle forces (2% of all studies)	Winby et al. 2009	Healthy subjects Comfortable gait speed vs. fast gait speed vs. slow gait speed (-)	Medial compartment loads were determined by activation of H, then activation of Q and in late stance by gastrocnemius. Lateral compartment loads were determined similar, except with contribution of the tensor fascia latae muscle.

3.12. Recent developments

Two studies by Farrokhi et al. [16,28] measured knee contact point movements during challenged (downhill) gait in patients with KOA and healthy control subjects. Knee contact point movements (and velocities) were estimated using dynamic stereo X-ray recordings (and additional CT-images) of the kinematics. Higher contact point movements and velocities were observed in patients with KOA compared to control subjects [28] and in patients with KOA-I compared to patients with KOA-S and control subjects [16].

Another recent study, by Morgan et al. [31], used a frequency based method from control theory to assess the stability of ACL patients called: the Nyquist and Bode criteria. In this method, gain and phase margins were calculated from the knee angles (measured with marker-based recordings). The knee was classified as unstable if both the gain and phase margin were negative and in which the deviation from zero of the phase margins indicated the amount of instability. Patients with an ACL injury were shown to be less stable at heel strike during comfortable gait (lower phase margins, larger deviation from zero) compared to controls. Moreover, the uninjured leg was more stable compared to healthy control legs at 15% and 30% of the stance phase.

Lastly, a study by Van den Noort et al. [25] presented a new method to measure responses to gait perturbations, called the gait sensitivity norm (GSN). The GSN is a method originated from the robotics field, where the response to a perturbation of one or several parameters measured with gait analysis is captured (for example response in knee angles). A higher GSN indicates a larger response to the perturbation, e. g. a more unstable knee. Van den Noort et al. [25] performed a pilot study and showed in nine healthy subjects that the GSN is feasible in measuring the responses to perturbations during gait. Higher GSN values were observed at increased intensities of the perturbation and lower GSN values after a number of steps following perturbation.

4. Discussion

The aim of this literature review was to make an inventory of the objective parameters used for knee joint (in)stability during gait. Eighty-nine studies were considered eligible, in which 33 different objective parameters were identified for comfortable gait, challenged gait or both. A majority of these parameters were based on kinematics (14 parameters), or electromyography (12 parameters) measurements. Forty-four per cent of the studies used a challenging gait condition to provoke knee instability. Limited, or conflicting results inhibited to recommend any of those parameter(s) as a clinically relevant (valid) and reliable objective measure for knee joint stability during gait.

The use of so many different parameters, reflecting 33 different interpretations of knee stability during gait, clearly demonstrates that a broad spectrum of measures has been explored. However, it also reveals the lack of a clear and well-accepted definition for knee joint stability during gait. This absence of a definition makes it difficult to develop an clinically relevant stability measure. The validity of such a measure needs to be proven, but since there is no such thing as a “golden standard” to validate a new measure against, studies are compelled to look at other levels of validity. In this review, studies looked for example at the ability to discriminate “stable” from “unstable” patients (previously divided in groups based on self-reported knee instability) [8,9,11,16,20,36,41,62,87,88,95] or the sensitivity of an intervention that is believed to be effective in improving knee stability [6,43,49–51,57–59,68,83,100]. Unfortunately, the evidence of validity for the measures inventoried in this review was too limited or conflicting to recommend any of those as stability measure(s). Therefore, consensus on the definition of dynamic knee joint stability is needed, enabling to focus future research directions into exploring and validating potential stability measures that are in line with this harmonized definition.

Studies that used similar parameter(s) for knee stability during gait were difficult to compare, due to differences in study populations (14 in this overview), disease or disease progression. Moreover, variable experimental designs, data processing and analysis limited fair comparisons. For example, differences were observed in experimental setups to obtain the kinematics (e.g. marker placement, measurement equipment) [42,75], the selection of muscles measured with EMG [52,77] and the processing of EMG signals (e.g. filtering, normalisation) [76,82]. Future studies investigating dynamic knee joint stability should therefore not only focus on testing the validity of their developed metrics but also on the ability to assess the test-retest and the inter-laboratory reliability of these metrics. Therefore, close collaboration between lab and research groups investigating the same patient populations is strongly needed, aiming to evaluate the inter-laboratory reliability of the knee stability measures [106] and to align the measurement protocols and data analysis methods accordingly. This will enable fair comparison between studies and establish the clinimetrics.

We are convinced that a future conceptual definition of knee joint stability would require a challenge during gait to provoke knee stability. Considering that comfortable walking allows compensation mechanisms, that will obscure the effects of instability. Any stability measure arising from comfortable gait would be less sensitive. Currently, challenged gait is increasingly explored (44% of all studies in this review), but it is unknown which type of challenge is most successful in provoking the largest response of knee instability. Fortunately, recent technological developments in gait analysis yielded instrumented treadmills making it feasible to apply different types of controlled perturbations [25]. Besides this, it seems likely that a future measurement of knee joint stability need to be based on a combination of measurements. A reason for this is that the parameters investigated in this review emerge from various domains, with the majority from kinematic and electromyography measurements. Furthermore, these parameters are often combined to form new parameters like the co-contraction index (combining multiple muscles) [6,11,24,37,47,50,52,77,80] or the gait sensitivity norm (combining several parameters in response to a perturbation) [25]. Based on the results of this review, we therefore suggest a new, broad definition for dynamic knee stability during gait to enhance the development of a stability measure: “*The capacity to respond to a challenge during gait within the natural boundaries of the knee.*”

Further efforts are needed to refine this definition and enable development of a reliable and clinically relevant measure for knee joint stability during gait. A possible first step might be to carry out an exploratory study in which the kinematics, kinetics and muscle activations are compared between healthy controls and different patient groups (e.g. in patients with KOA and self-reported ‘stable’, or ‘unstable’ knee(s)) during comfortable and challenged gait. A range of gait challenges can then be applied. Several (combinations) of objective parameters can be explored to quantify the response to a challenge in each group, with the healthy control group setting the natural boundaries of the knee (i.e. the physiological response from a healthy knee). Selection of an appropriate candidate(s) as a measure for knee joint stability during gait will be driven by their ability to discriminate groups in this study. Further efforts will then be required to test validity and reliability on the developed stability measure(s). These include, correlation with self-reporting; sensitivity to interventions with known effects (e.g. knee braces [35,105] or muscle strengthening [34]); and test-retest reliability. All of these goals will require efforts from groups from the international community. Therefore, studies that compare protocols and consensus are required to align protocols and data analyses to compare between studies from different laboratories and/or lump their data. Eventually this will provide evidence for utilization of a selected stability measure in clinical practice.

This literature review has some limitations. First, the studies are based on gait analysis in a laboratory environment. Walking in a lab is different than in real life [107]. However, the standardized setting makes it possible to evaluate gait performance in a controlled environment, that will optimize the comparison between studies. Second, this literature review only focused on knee stability during walking. Therefore, it excluded alternatives for knee (in)stability during other dynamic activities (e.g. to negotiate stairs or to raise from a chair). Nevertheless, gait is the most common task in which patients reported knee joint instability [10] and in most cases these patients also reported knee joint instability during other dynamic tasks [10]. Finally, there were some limitations of the methods of this review: the selection of the abstracts and the data extraction were performed by one author. The main concern could be that eligible studies will be missed, but we tried to minimize this by double checking all references of each included study.

5. Conclusion

It can be concluded that many different concepts of knee joint stability during (challenged) gait are reported in literature. These are presented as many different objective parameters without emphasis on one specific parameter. To enable development of a clinically relevant measure for knee joint stability, consensus needs to be reached by the international research community on the concept and definition of knee joint stability during gait. To start off, we suggest : “The capacity to respond to a challenge during gait within the natural boundaries of the knee”. At the same time, there is an urgency for research groups to agree on experimental protocol harmonization. These efforts are needed before the next step can be taken, i.e. to make fair comparisons of stability parameters (that comply to the agreed definition) between studies. Reliability and validity of such candidates for stability measures can then be evaluated, yielding an decided parameter to assess knee joint instability.

Conflict of interest

The authors confirm that there are no conflict of interest regarding the work described in the current manuscript.

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