The influence of the irrigating solution on articular cartilage in arthroscopic surgery: A systematic review

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ABSTRACT

Purpose: Arthroscopic surgery has become an important and popular orthopedic procedure for numerous joint disorders. Continuous irrigation is performed to replace synovial fluid for optimal joint distension and clear visualization of the synovial cavity. Irrigation solutions may, however, negatively impact articular cartilage and chondrocyte viability. This systematic review aims to compare different irrigating solutions and their properties to determine whether one is superior in its effects on articular cartilage and chondrocytes.

Methods: A systematic literature review was conducted. The online databases: Embase, Medline, HealthStar, Emcare and PubMed were searched from 1946 to August 2018. Methodological index for non-randomized studies (MINORS) was used to assess methodological quality of the included studies.

Results: Sixteen studies met the inclusion/exclusion criteria and were included in this review. Although the studies used different criteria to define superiority, solution superiority was based on results that focused on articular cartilage and chondrocyte viability. Seven of the sixteen included studies compared Ringer's/lactate solution or Ringer's lactate to normal saline. Three found Ringer's solution or Ringer's lactate to be superior to saline, whereas, three studies found no significant differences and one study found Ringer's lactate to be inferior to saline only when their osmolarities differed. Four studies compared ionic to non-ionic solutions. Two of the four studies demonstrated non-ionic solutions to be superior, one had demonstrated no significant differences between solutions, while one had mixed results. Six of the sixteen included studies compared differing osmolarities. One found no statistically significant differences between solutions of differing osmolarities, whereas, the remaining five studies found superiority with hyperosmolarity. Two of the sixteen included studies examined the effects of different temperatures. Both studies concluded that the use of a warmer (more physiological) temperature is more ideal. Two of the sixteen studies included in this review compared solutions with differing pH levels. Both studies concluded on the importance of utilizing the more physiological solutions for arthroscopic procedures.

Conclusion: Ringer's Lactate and Ringer's Solution as well as non-ionic solutions may have merit over the use of the normal saline for irrigation. Hyperosmolarity, warmer solutions and ones with more physiological pH values may be beneficial when considering potential effects on articular cartilage and chondrocytes. The current review demonstrated trends found in the current literature, which require human studies – preferably high quality RCTs – to make recommendations that aid surgeons in making the best decision regarding the ideal irrigation solution to use on their patients.

Level of evidence: Level IV, Systematic review of Level IV studies.

1. Introduction

Arthroscopic surgery has become an important and popular orthopedic procedure for numerous joint disorders. Continuous irrigation is performed in order to replace synovial fluid for optimal joint distension and clear visualization of the synovial cavity. Normal knee synovial fluid characteristics include a pH of 7.7 and an osmolarity of 404 mOsmols/L¹ (Table 1). When synovial fluid is replaced with an irrigation solution, alterations in the ideal environment occur promptly,² due to changes to temperature, osmolarity, pH, and oxygen saturation.² Since articular cartilage is dependent on the synovial fluid for its nutrition, it is sensitive to these changes.^{3,4} Irrigation fluids used during arthroscopic surgery may result in increased elimination of proteoglycans out of the tissue, subjecting articular cartilage to potential

mechanical injury⁵ and resulting in matrix degradation and chondrocyte death.^{6–8} Articular cartilage chondrocytes are, however, crucial to the synthesis of the proteoglycan and collagen of the extracellular matrix, as well as the essential enzymes for building and degrading them. As a result, injury to articular cartilage chondrocytes is undesirable and should be mitigated.

Is there an irrigation solution capable of minimizing risks to the articular cartilage? Although normal saline is a commonly used irrigation fluid in arthroscopic surgery, Shinjo et al. has claimed worse maintenance of human meniscus cell integrity with its use, when compared with Ringer's solution.⁹ Other commonly used irrigation fluids include ionic solutions such as Ringer's Solution and Lactated Ringer's Solution as well as non-ionic solutions such as Manitol Solution, Sorbitol Solution, Dextrose Solution, Dextran Solution, and

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Table 1
Fluid characteristics and types of fluids.

Fluid	Average pH (range)	Osmolarity	Composition
Synovial Fluid	7.7	404 mOsmol/L	Hyaluronic Acid
Ionic			
Normal Saline ^a	5 (4.5–7)	308 mOsmol/L	Sodium and Chloride
Ringer's Solution ^a	5.5 (5–7.5)	309 mOsmol/L	Sodium, Chloride, Potassium and Calcium
Lactated Ringer's Solution ^a	6.5 (6–7.5)	273 mOsmol/L	Sodium, Chloride, Potassium, Calcium and Lactate
Non-Ionic			
Mannitol 5% ^a	5.5 (4.5–7.0)	275 mOsmol/L	Mannitol
Mannitol 10% ^a	5	549 mOsmol/L	Mannitol
Sorbitol 3% ^a	5.0 (4.5–6.5)	165 mOsmol/L	Sorbitol
Dextrose 5% ^a	4	252 mOsmol/L	Dextrose
Dextran 6% ^b	4.5	300 mOsmol/L	Dextran
Glycine 1.5% ^b	6.0 (4.5–6.5)	200 mOsmol/L	Glycine

^a Data obtained from Baxter Healthcare Corporation, Round Lake, IL.

^b Data obtained from Sigma-Aldrich Inc, St. Louis, MO.

Glycine Solution. Would a different ionic solution, such as Ringer's lactate, have better outcomes or should irrigation be carried out with the use of a non-ionic fluid? Furthermore, are there specific temperatures, pH levels, or osmolarities that would result in more optimal conditions with chondroprotective effects for reducing potential damage to articular cartilage?

The present review aims to compare and contrast the effects of different irrigation fluids, and differences in fluid properties, on articular cartilage and determine whether one is superior in its effects, in order to help surgeons performing arthroscopic procedures to make clinical decision aligned with the most current best available evidence. We hypothesize there is a solution that has minimal detrimental effects on the articular cartilage and will be an ideal solution to be used in arthroscopy. To the best of our knowledge, this is the first such review of its kind.

2. Materials and methods

2.1. Search strategy

Two blinded reviewers independently searched the online databases: Embase, Medline, HealthStar, Emcare and PubMed from 1946 to August 2018, for literature addressing irrigating solutions for arthroscopic procedures and their effects on articular cartilage. The research question and the inclusion and exclusion criteria were decided on a priori. The key terms: “Arthroscopy”, “Arthroscopic”, “Irrigation solution”, and “Irrigation fluid” were used.

Duplicate screening was carried out for the titles, abstracts, and full text. Discussion between two reviewers took place to address disagreements, and if needed, the senior author resolved issues related to study selection. Studies were included if they contained: [1] irrigating solutions; [2] implications for/focus on arthroscopy; [3] examination of the effects on articular cartilage/chondrocytes [4] joints of the extremities; [5] comparison(s) of different solutions or the same solution with different properties (such as temperature, osmolarity, or pH); [6] primary article; [7] short term exposure to irrigation fluids; and [8] full text. The following components were made part of the exclusion criteria: [1] studies lacking a comparator group; [2] studies without an arthroscopic focus; [3] studies focusing on epinephrine/nor-epinephrine; [4] studies focusing only on electrosurgery in arthroscopy; [5] studies not examining the effects on articular cartilage or chondrocytes; [6] studies that are not available or full-text not accessible; [7] conference proceedings or abstracts; and [8] literature reviews and case reports.

Methodological index for non-randomized studies (MINORS) is a

valid 12-item instrument that is used to assess the quality of non-randomized surgical studies. The global ideal score for these comparative studies is 24.¹⁰

2.2. Data abstraction

The two reviewers abstracted the data in duplicate and kept the records in a Microsoft Excel 2010 spreadsheet. The data included: year of publication, author, location of study, study design, follow-up intervals, participants or specimens used, type of treatment/intervention, results, and outcome measures.

2.3. Statistical analysis

An intraclass correlation coefficient was used for agreement between reviewers on MINORS scores. For all phases of the abstract and full text screening, a weighted kappa (κ) was calculated to assess inter-rater agreement.¹¹ The following kappa values were selected a priori: $\kappa > 0.61$ to signify substantial agreement; $0.21 < \kappa < 0.60$, to signify moderate agreement; and $\kappa < 0.20$, to signify slight agreement.¹¹ Descriptive statistics were reported for the studies included in this review.

3. Results

In reviewing the literature, 1845 studies were identified. Duplicates were excluded, leaving 1032 studies to be screened. Further, 933 studies were excluded based on the title screen. 76 studies were excluded based on the abstracts. 7 studies were excluded based on the full text screen. Sixteen studies met the inclusion criteria and were included in this review.^{12–27} This number is inclusive of the studies found after screening the reference sections of the initial studies (Fig. 1).

MINORS scores of the included studies ranged between 13 and 17, with a mean score of 15.75 (Table 2). There was high agreement between reviewers regarding quality assessment scores, with an intraclass correlation coefficient of 0.95 (95% confidence interval, 0.86 to 0.96).

At both the abstract and full text stages, reviewers had considerable agreement when selecting which articles to include, with $\kappa = 0.99$ (4 of 1265 articles in disagreement) and $\kappa = 1$, respectively. The senior author was not required to resolve inconsistencies.

Due to the heterogeneity among the studies, a meta-analysis and a quantitative analysis were both not possible. A qualitative analysis of the included studies is summarized in Table 3.

3.1. Ringer's Lactate and Ringer's solution vs normal saline

Seven of the sixteen included studies compared Ringer's solution or Ringer's lactate to normal saline.^{12–18} Three of the seven studies^{12–14} found Ringer's solution or Ringer's lactate to be superior to saline in terms of cartilage health, measured by cartilage metabolism; whereas, three studies^{15–17} found no significant differences between solutions. The remaining study, Amin et al.,¹⁸ found Ringer's lactate to be inferior to saline when their osmolarities differed. Using confocal laser scanning microscopy, Amin et al. found greater chondrocyte death of injured cartilage in the superficial zone when utilizing Ringer's lactate versus normal saline; however, when osmolarities were increased and comparable between these irrigation fluids, chondrocyte death lessened and there were no significant differences between the two solutions.¹⁸ Upon measuring radiolabeled sulfate (³⁵SO₄) uptake to assess cartilage metabolism, Guilhar et al. and Bulstra et al. determined Ringer's solution to have the least cartilage metabolism inhibition, when compared to normal saline.^{12,14} Reagan et al. concluded that normal saline is not physiological and inhibits chondrocyte proteoglycan synthesis compared with Ringer's lactate, after assaying radioactivity of specimens.¹³ Another study that measured ³⁵SO₄ uptake rate found no significant differences between Ringer's lactate and normal saline with regard to

Fig. 1. Flow diagram of studies found.

proteoglycan synthesis.¹⁶ In a scanning electron microscope study, Yang et al. found no significant differences in specimen surface ultrastructure between Ringer's lactate and normal saline.¹⁵ Finally, Grading et al. reported that proteoglycan content released from the cartilage was highest among Ringer's lactate and normal (0.9%) saline, with no significant differences noted between the two solutions.¹⁷

3.2. Ionic vs non-ionic

Four of the sixteen included studies compared ionic versus non-ionic solutions^{12,15,17,19} (Table 1). One study¹² had mixed results, with Ringer's lactate (ionic) superior to all non-ionic solutions; however, these non-ionic solutions were superior to normal saline (ionic), with saline demonstrating the greatest inhibition of cartilage metabolism when measuring radiolabeled sulfate (³⁵SO₄) uptake. Two of the four studies demonstrated non-ionic solutions to be superior.^{17,19} Via indentation creep testing, Jurvelin et al. found that the greatest and earliest cartilage softening had occurred with Ringer's solution versus the non-ionic solutions, mannitol (5%) or fructose (5%).¹⁹ The study by Grading et al. demonstrated that ionic solutions, such as Ringer's lactate, resulted in greater proteoglycan loss, with rougher and more uneven cartilage surfaces (using a scanning electron microscope) when compared with non-ionic solutions, such as mannitol.¹⁷ Lastly, one study found no significant differences in the surface ultrastructure of cartilage between ionic (Ringer's lactate and normal saline) and non-ionic solutions (3% sorbitol and distilled water).¹⁵

3.3. Influence of osmolarity

Six of the sixteen included studies compared the results of irrigation solutions that had differing osmolarities.^{18,20–24} One out of the six studies²⁰ that analyzed irrigation fluids during canine shoulder arthroscopy found no statistically significant differences between normal saline and a hyperosmolar irrigation fluid when examining changes in

shoulder girth, tissue water content, or chondrocyte viability. The remaining five studies found superiority with hyperosmolarity.^{18,21–24} Amin et al. determined that increasing osmolarity reduced chondrocyte death of injured cartilage in the superficial zone, which was examined via confocal laser scanning microscopy.¹⁸ In one study,²¹ articular cartilage exposed to the hyperosmotic saline solution had a six-fold ($p = 0.04$) decrease in chondrocyte death, after mechanical injury to the articular cartilage, when compared with normal saline using confocal laser scanning microscopy. Again, with the use of confocal laser scanning microscopy, Amin et al. found that greatest cell death for wounded articular cartilage occurred at 0 mOsm/L; whereas, chondroprotective effects were noted at higher osmolarities (480 mOsm/L).²² In injured human articular cartilage, Huang et al. used laser confocal scanning microscopy and a spectrophotometer to demonstrate that with increased osmolarity, the percentage of cell death and proteoglycan elution was reduced.²³ Finally, results from a study by Eltawil et al. found, via confocal microscopy, that hyperosmotic saline resulted in a significantly lower percentage of chondrocyte death, as well as improved repair score, injury width, and type II collagen and aggrecan levels, when compared with normal saline.²⁴

3.4. Influence of temperature

Two of the sixteen included studies examined the effects of different temperatures of irrigation solutions.^{25,26} Both studies concluded that the use of a warmer (more physiological) temperature is more ideal. Kocaoglu et al. found significantly lower RNA yield, lactate production, and proteoglycan content in the porcine osteochondral explants from juvenile pigs exposed to the lower temperatures (4 and 24° Celsius) than with the higher temperature groups (32 and 37° Celsius).²⁵ In the study by Cheng et al., the rat knee articular cartilage irrigated with fluids closer to body temperature showed more even surfaces and no fibril exposure; whereas, those irrigated with cold fluids (4° Celsius), demonstrated uneven surfaces and fibril exposure.²⁶ The two studies

Table 2
MINORS scoring of included studies.

	Gulihar et al. 2013 ¹²	Reagan et al. 1983 ¹³	Bulstra et al. 1994 ¹⁴	Yang et al. 1993 ¹⁵	Arciero et al. 1986 ¹⁶	Grading et al. 1995 ¹⁷	Amin et al. 2010 ¹⁸	Jurvelin et al. 1994 ¹⁹	Capito et al. 2015 ²⁰	Amin et al. 2011 ²¹	Amin et al. 2008 ²²	Huang et al. 2015 ²³	Eltawil et al. 2015 ²⁴	Kocaoğlu et al. 2011 ²⁵	Cheng et al. 2004 ²⁶	Akgun et al. 2014 ²⁷
1. A clearly stated aim	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
2. Inclusion of consecutive patients	1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	N/A	1	N/A	N/A	N/A	N/A
3. Prospective collection of data	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
4. Endpoints appropriate to the aim of the study	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
5. Unbiased assessment of the study endpoint	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6. Follow-up period appropriate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
7. Loss to follow up less than 5%	0	0	0	2	1	0	2	1	0	0	2	0	0	0	0	2
8. Prospective calculation of the study size	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9. An adequate control group	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
10. Contemporary groups	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
11. Baseline equivalence of groups	1	1	1	2	1	1	1	1	2	1	1	1	1	1	2	1
12. Adequate statistical analyses	2	0	2	0	2	2	2	2	2	2	2	2	2	2	2	2
Total Score/24	16	13	15	16	16	15	17	16	16	16	17	16	15	15	16	17

The items are scored: 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).

Table 3

Summary of results of included studies - Outcome(s) of interest, outcome Measure(s) and superior fluid findings.

Study	Outcome(s) of interest	Outcome measure(s) used	Qualitative Assessment (Superior fluid when examining effects on articular cartilage)
Gulihar et al. 2013 ¹²	Proteoglycan synthesis, cartilage metabolism	Measured radiolabeled sulfate (³⁵ SO ₄) uptake	Ringer's solution > 1.5% glycine > 5% mannitol > normal saline > 0.5% bupivacaine
Reagan et al. 1983 ¹³	Proteoglycan synthesis, cartilage metabolism	Assayed for incorporated radioactivity: radiolabeled sulfate (³⁵ SO ₄)	Ringer's lactate and acetate > normal saline and phosphate-buffered saline
Bulstra et al. 1994 ¹⁴	Proteoglycan synthesis, cartilage metabolism	Measured radiolabeled sulfate (³⁵ SO ₄) uptake	Ringer's solution > Ringer's glucose > Ringer's lactate = normal saline
Yang et al. 1993 ¹⁵	Effects on ultrastructure of articular cartilage	Scanning electron microscope	Ringer's lactate = normal saline = distilled water = 3% sorbitol
Arciero et al. 1986 ¹⁶	Effects on chondrocyte metabolism	³⁵ SO ₄ incorporation rate by articular cartilage	Normal saline = Ringer's lactate = sterile water
Grading et al. 1995 ¹⁷	Effects on cartilage ultrastructure Differences in proteoglycan extraction	Viewed surface ultrastructure using scanning electron microscope Chondroitin sulfate a calibration curve Aliquots of fluid assayed	5% mannitol solution > Ringer's solution = normal saline
Amin et al. 2010 ¹⁸	Chondrocyte death	Confocal laser scanning microscopy	Ringer's lactate = normal saline, when osmolarities were the same (600mOsm) When osmolarity of saline is greater: normal saline (285 mOsm) > Ringer's lactate (255mOsm) 5% mannitol = 5% fructose > Ringer's solution
Jurvelin et al. 1994 ¹⁹	Tissue degeneration	Indentation creep testing	
Capito et al. 2015 ²⁰	Chondrocyte viability	Visualization was carried out with images taken of the staining using a fluorescent microscope and area was measured using MicroSuite Basic edition software program	Normal saline = hyperosmolar irrigation fluid
Amin et al. 2011 ²¹	Chondrocyte death	Confocal laser scanning microscopy	Hyperosmotic saline > normal saline
Amin et al. 2008 ²²	Chondrocyte death	Confocal laser scanning microscopy	480 mOsm > 0 mOsm
Huang et al. 2015 ²³	Chondrocyte survival and metabolic state	Laser confocal scanning microscopy, TUNEL assay, Spectrophotometer	Higher osmolarity > lower osmolarity
Eltawil et al. 2015 ²⁴	Percentage of cell death Repair from injury	Confocal microscopy Histology/immunostaining	Hyperosmotic saline (600 mOsm) > normal saline
Kocaoglu et al. 2011 ²⁵	Chondrocyte metabolism and RNA synthesis	RNA yield analysis and proteoglycan content and lactate production	Higher temperatures (32 and 37° Celsius) > lower temperatures (4 and 24° Celsius)
Cheng et al. 2004 ²⁶	Effect on articular cartilage surface	Specimens were viewed with a scanning electron microscope	Fluid closer to body temperature (37° Celsius) > colder fluid (4° Celsius)
Akgun et al. 2014 ²⁷	Changes in cartilage metabolism	RNA yield analysis	pH closest to physiological pH (7.4) > either acidic or basic (7.2 or 7.6)

found less suppression of chondrocyte metabolism with the warmer temperatures.^{25,26}

3.5. Influence of pH

Two of the sixteen studies included in this review compared solutions with differing pH levels.^{13,27} Reagan et al. demonstrated mixed results. Although phosphate-buffered saline initially showed a rise in incorporation of ³⁵SO₄ (increased metabolic activity), these increments ultimately fell and Ringer's lactate (pH = 6.3) and Ringer's acetate (pH = 6.3) were superior to both normal saline (pH = 5.3) and phosphate buffered saline (pH = 7.1) in supporting metabolic activity.¹³ The study by Akgun et al. found that exposure to solutions that are either acidic or basic affect chondrocyte activity, with even a difference of 0.2 unit from normal pH resulting in suppression of RNA synthesis and chondrocyte metabolism.²⁷ Both studies concluded on the importance of utilizing the more physiological solutions for arthroscopic procedures.^{13,27}

4. Discussion

The need for and safety of utilizing a fluid medium has been well documented in orthopedic literature, particularly when it comes to examining the effects on articular cartilage and chondrocytes. Farr et al. found that within 2 h of an open surgical procedure, chondrocyte viability is significantly higher when treated with a saline drip or other medium, compared with no hydrating treatment solution to exposed cartilage.²⁸ To maintain chondrocyte viability, a specific recommendation in the literature suggests that exposed cartilage should be hydrated every 10–20 min with lactated Ringer's solution.²⁹

Nevertheless, it is crucial to utilize the 'ideal' fluid for the procedure at hand. Douw et al. demonstrated this with case reports of six knees that had accidentally been irrigated with chlorohexidine, a fluid commonly used in the preparation of surgical wounds and not an irrigation solution normally used in arthroscopy, with a portrayal of its deleterious effects on articular cartilage.³⁰ All knees developed swelling, persisting pain, crepitus, and decreased range of motion. Examinations via radiographs and histology exhibited loss of joint space from chondrolysis, with synovitis and loose bodies, cartilage necrosis, and fibrosis of synovial specimens.³⁰ Such is an extreme example of what may occur when the wrong or non-ideal fluid is utilized.

4.1. Ringer's solution and Ringer's lactate vs. normal saline

Normal Saline and Ringer's lactate/Ringer's solution contain sodium, chloride, potassium and calcium, but Ringer's lactate has lactate added to it. Although maintaining different compositions, Ringer's solution and Ringer's lactate have been grouped together due to the limited number of studies and the lack of comparison between the two.

When comparing normal saline to Ringer's solution and Ringer's lactate, this review finds the latter group to be preferable, since the studies examined either found Ringer's solution and Ringer's lactate to be superior or equivalent to normal saline. Such a preference for Ringer's solution and Ringer's lactate could be due to specific differences in the fluids' properties (Table 1). Normal saline (0.9%) has an average pH of 5 and potentially as low as 4.6.³¹ Ringer's lactate has an average pH of 6.5, with similar electrolytes as plasma.³² Maroudas also described the electrolyte activity of articular cartilage as similar to that of Ringer's solution.³³ It could, therefore, be these properties that make Ringer's solution and Ringer's lactate more physiological, hence, apt to

less deleterious effects on articular cartilage when compared with normal saline.

Preference of irrigating with Ringer's lactate over normal saline has also been demonstrated when studying their effects on surrounding tissue, with better preservation of meniscal cell integrity using the former.⁹ Utilizing flow cytometry, Chu et al. determined that 60 min post-exposure to normal saline, 35% of chondrocytes were dead or apoptotic.³⁴ Similarly, Karpie et al. found 20% of chondrocytes were either dead or apoptotic after 1-h exposure with normal saline.³⁵

4.2. Ionic vs. non-ionic

Results as to whether the ideal irrigating solution should be ionic versus non-ionic were mixed but demonstrated potential benefits of non-ionic solutions. Nevertheless, Ringer's solutions (ionic) also demonstrated merit within the included studies, and the use of ionic solutions has been more widespread, with more studies determining their safety and efficacy during arthroscopic procedures.

When examining the literature on related topics, Reagan et al. concluded that the non-ionic glycerol (2.6%) would be the best solution to use for arthroscopy with electrosurgery, not only because it is safe, but since it supported cartilage metabolism for 2 h.³⁶ The issue with Ringer's lactate and normal saline in this study was the fact that they were too conductive, which could be expected when dealing with electrosurgery; however, this would not be a concern with a standard arthroscopic procedure, the focus of this review. The included study by Gradinger et al. showed that a saline concentration of 0.1% did not result in the proteoglycan loss that occurred with normal saline (0.9%), which may demonstrate that proteoglycan extraction from cartilage occurs with higher ionic concentrations.¹⁷

Non-ionic 1.5% glycine has been used for arthroscopy and has been investigated by one of the studies included in this review¹²; nevertheless, intravascular absorption of large volumes has been documented to potentially cause visual, renal, neurologic and cardiovascular disorders, as well as fatal water intoxication leading to cerebral edema.^{37–41} Although these negative side-effects are not directly related to our primary focus of the effects on articular cartilage, they are still crucial to consider when selecting an ideal solution.

4.3. Osmolarity

Chondrocytes need to endure an environment of low osmolarity for the duration of the procedure and until synovial fluid is re-established, since solutions generally used for irrigation, such as lactated Ringer's (273 mOsm/L) and saline (0.9%, 308 mOsm/L), have mean osmolarities lower than synovial fluid (404 mOsm/L).⁴²

Increased osmolarity leading to chondroprotective effects is a conclusion that most of the included studies agreed with.^{25,28–31} Previous studies have also demonstrated that after mechanical injury to the articular cartilage, a decrease in extracellular osmolarity resulted in more extensive chondrocyte death compared with a higher osmolarity.^{43,44} One study found that during drilling, chondrocyte death was significantly reduced by raising osmolarity and reducing Ca²⁺ content.⁴⁵

The results in the included study by Amin et al. showed that the effects of medium osmolarity are most pronounced in the superficial zone due to cell volume, with the superficial zone containing the most water content and permeability.²¹ As a result, the chondroprotective mechanism of high osmolarity may be water efflux from cells, causing decreased chondrocyte volume.²¹ Overall, such positive effects with hyperosmolar solutions have even translated into clinical improvements, as a recent double-blind, randomized controlled trial demonstrated that human participants had significantly less pain, change in extremity girth, and mean weight gain with the hyperosmolar group compared with the isotonic group.⁴⁶

4.4. Temperature

Both studies focusing on differing temperatures examined in this review demonstrated the positive effects of a warmer solution, particularly the lower chondrocyte metabolism suppression. Nevertheless, limited studies have been conducted, and so, for a firm recommendation to be made, such studies are ultimately warranted. Although colder solutions have been recommended for use with arthroscopic procedures to reduce post-operative inflammation and pain^{47,48}, other studies have suggested otherwise. Pan et al. had recommended warm irrigations fluids for arthroscopic shoulder surgery based on their findings that warmer solutions resulted in significantly reduced local inflammatory responses and hypothermia.⁴⁹ Similar beneficial findings had been noted by Parodi et al., with warmed irrigating solutions used during hip arthroscopy reducing the risk of decreased core body temperature.⁵⁰ Furthermore, one study found that irrigation with a cold solution (colder than body temperature) has resulted in human meniscal changes,³ and it would be useful, for our purposes, to know whether one might expect the surrounding tissue to demonstrate such detrimental changes as well.

4.5. pH values

Jebens and Monk-Jones suggested that irrigation solutions with a pH around 6.5 would not be physiologic to articular cartilage tissue, which is the average pH of irrigating solutions commonly used.¹ They showed synovial fluid to have a pH of 7.7, a value higher than even blood pH.^{1,51} The studies examining pH in this review demonstrated that having a pH close to physiological pH would be ideal^{13,27}; however, it is evident that other properties/factors, such as a solution's ionic make-up, may trump the importance of pH and these other factors would then have to be considered in addition to the solution's pH. A further consideration would be the question of whether a more basic or a more acidic pH would result in greater damage to articular cartilage and should be examined in future studies. Nevertheless, one study determined that cell death was at 8.4% with the phosphate-buffered saline control group, and chondrocyte death was only increased when the pH of phosphate-buffered saline was at or below 3.4.⁵² On the other hand, Karpie and Chu used flow cytometry to determine chondrocyte viability and did not find any significant differences with the use of normal saline at different pH levels (5.0, 7.0, 7.4).³⁵ These results would be contradictory to the results in the included study by Akgun et al., who demonstrated a difference in chondrocyte metabolism with only a change of 0.2 in pH.²⁷ Ultimately, further studies addressing this topic are warranted.

4.6. Other factors

When examining the effects of arthroscopic surgery on articular cartilage, other factors may also be considered to determine the optimal procedural conditions. Shen et al. found that utilizing normal saline with 110 mm Hg pressure at room temperature for 45 min or longer (their standard arthroscopic procedure conditions) resulted in a significantly lower chondrocyte viability compared with baseline status, in cartilage specimens harvested from the femoral notch. Reduction of operation times was suggested to minimize these detrimental effects on articular cartilage.⁵³ Additionally, irrigation systems themselves influence the outcome of arthroscopy with regards to articular cartilage and other tissue.⁵⁴

4.7. Limitations

In addition to the limitations stated within the body of this discussion, other limitations of this review should be noted. We were unable to perform meta-analysis due to the heterogeneity of results and outcome measurements utilized for comparison. The number of studies in

each sub-topic examined were limited and the studies used generally had a small number of participants/subjects/explants, poor study designs (preclinical studies and not the gold standard of an RCT), and a short-term focus. Most of the studies utilized animal specimens/explants and examinations were performed in vitro. Furthermore, the interventions across studies had differed, and so, even when making comparisons, such ionic versus non-ionic, the non-ionic solutions utilized were different across studies.

5. Conclusion

This review aimed to determine whether there is an ideal irrigating solution for arthroscopic procedures, which minimizes any potential damage to articular cartilage and chondrocytes in humans. When considering potential effects of articular cartilage and chondrocytes, Ionic Ringer's Lactate and Ringer's Solution as well as non-ionic solutions may have merit over the use of the ionic normal saline for irrigation. Hyperosmolarity has potential chondroprotective effects. Further, warmer solutions and ones with more physiological pH values may be beneficial when considering potential effects on articular cartilage and chondrocytes. The literature did not strongly identify which variable is the most important. Since the studies included in this review had a high degree of variability with most of them being in vitro or animal studies, it is important to be cautious when making suggestions regarding the viability of articular cartilage or making clinical decisions based on these data. The current review demonstrated trends found in the current literature, which require human studies – preferably high quality RCTs – to make recommendations that aid surgeons in making the best decision regarding the ideal irrigation solution to use on their patients.

Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jor.2019.02.018>.

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