

## Supplement File 4. Complete survey questions and invitation

### **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

Dear Colleague,

Thank you very much for taking the time to answer this online survey on global attitudes and practices relating to Sperm DNA Fragmentation testing and management. With the continuous evolving research on SDF, there is still a lack of implementation of this advanced sperm function test on clinical grounds. This global survey aims to investigate the clinical utility of SDF testing.

This survey is an attempt to understand how the medical experts around the world view and manage sperm DNA fragmentation, how these practices may differ amongst experts, and from official guidelines or recommendations based on systematic reviews. Identifying areas of divergent opinion would help us identify those areas needing further research to achieve consensus on the best management for our patients.

The survey may take between 20 to 30 minutes and is a little long as it seeks to cover all aspects of practice related to sperm DNA fragmentation testing and management, but the results will help shape the direction of future research for standardizing evaluations and treatments to serve patients best. We hope you will be able to take the time to answer it in depth. By submitting your answers, you consent to participate in this survey.

Please note that your responses will not be saved as you go along, and you will need to complete the survey in one sitting.

The secure link to the online survey is:

<http://survey.clevelandclinic.org/TakeSurvey.aspx?SurveyID=n6M271900>

The survey link will remain open for two weeks. Please contact me (Ashok Agarwal, [agarwaa@ccf.org](mailto:agarwaa@ccf.org)), Dr. Keshab Karna ([karnak@ccf.org](mailto:karnak@ccf.org)), or Dr. Shinnosuke Kuroda ([kurodas2@ccf.org](mailto:kurodas2@ccf.org)) in case of any problem in accessing the survey. To avoid any problems in opening this survey, we strongly recommend that you use Google Chrome as an internet browser, instead of others such as Internet Explorer. Please, copy the survey link and paste the URL into the Google Chrome browser address bar.

Thank you once again for your time and contribution to this major academic activity; we plan to share the results of this survey when completed.

Sincerely,

Ashok Agarwal, Ph.D., HCLD  
Director Andrology Laboratory  
Director of American Center for Reproductive Medicine  
Professor of Surgery (Urology)  
Department of Urology  
Cleveland Clinic, Cleveland, Ohio, USA

## **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

### **SECTION I: Participant Demographics**

Abbreviations: SDF: sperm DNA fragmentation; ART: assisted reproductive technology; IUI: intrauterine insemination; IVF: in-vitro fertilization; ICSI: intracytoplasmic sperm injection; UMI: unexplained male infertility; IMI: idiopathic male infertility; RPL: recurrent pregnancy loss.

Instructions to participants: Please answer all questions. The option "Not Applicable" is available if you do not encounter such a case in your practice.

**1. Survey Participant's Name\***

First

Middle

Last

**2. Email Address\***

**3. In which country do you practice?\***

**4. How old are you (years)?**

- 25-34
- 35-44
- 45-54
- 55-64
- >65

**5. What is the nature of your employment?**

- Physician, attending
- Physician, fellow
- Physician, resident
- Advanced practice provider (Physician Assistant, Nurse Practitioner)
- Reproductive Biologist/Embryologist
- Researcher (Full-time)
- Other

**6. What is your area of specialization (as it relates to male infertility)?**

- Fellowship-trained reproductive urology
- General urology
- Gynecology
- Endocrinology
- Clinical andrologist

- ART specialist
- Primary care
- Clinical Laboratory
- Embryology/Biology
- Other

**7. What is your practice setting?**

- Academic
- Public
- Private
- Multiple
- Other

**8. How many years have you been practicing (related to male infertility)?**

- Less than 2 years
- 2-5 years
- 6-10 years
- 11-15 years
- More than 15 years

**9. On average, how many infertile couples do you manage per week?**

- ≤10
- 11-20
- 21-30
- 31-40
- 41-50
- >50

**10. How many IVF/ICSI full cycles (= oocyte pickup) are performed in one year at your center by your entire team?**

- ≤100
- 101-400
- 401-800
- >800
- I refer my IVF/ICSI couples to another center
- Not applicable

**11. What is the cost of SDF testing in your area?**

- Less than \$50
- \$50-100
- \$100-200
- \$200-500
- \$500-1000
- More than \$1000

## **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

### **SECTION II: Indications for SDF testing**

Abbreviations: SDF: sperm DNA fragmentation; ART: assisted reproductive technology; IUI: intrauterine insemination; IVF: in-vitro fertilization; ICSI: intracytoplasmic sperm injection; UMI: unexplained male infertility; IMI: idiopathic male infertility; RPL: recurrent pregnancy loss.

Instructions to participants: Please answer all questions. The option "Not Applicable" is available if you do not encounter such a case in your practice.

**12. Do you order SDF testing in couples with unexplained infertility?**

- Yes, in all cases
- Yes, in some cases
- No, due to lack of resources or facility to do the test
- No, as the results will not impact the treatment decision
- Not applicable

**13. When would you order SDF testing for men presenting with unexplained male infertility (UMI: no identifiable underlying cause for infertility and normal semen parameters)? [Select all that apply]**

- Routinely, as part of initial work-up after UMI is diagnosed
- After failure of empiric antioxidant or hormonal therapy
- Before referral for ART
- After failure of ART
- I do not order SDF testing for UMI
- Not applicable

**14. Do you order SDF testing for men with idiopathic male infertility (IMI: no identifiable underlying cause for infertility with abnormal semen parameters)?**

- Yes, in all cases
- Yes, in some cases
- No, due to lack of resources or facility to do the test
- No, as the results will not impact the treatment decision
- Not applicable

**15. When would you order SDF testing for men presenting with idiopathic male infertility? [Select all that apply]**

- Routinely, as part of initial work-up after IMI is diagnosed
- After failure of empiric antioxidant or hormonal therapy
- Before referral for ART
- After failure of ART
- I do not order SDF testing for IMI
- Not applicable

**16. For a couple with recurrent pregnancy loss (2 or more miscarriages) after natural conception, and a normal female partner, when will you order SDF testing? [Select all that apply]**

- Routinely, during initial work-up
- If initial work-up is unremarkable, with normal semen parameters

- If initial work-up is noticeable only for abnormal semen parameters
- After failure of empiric antioxidant or hormonal therapy
- Before referral for ART
- After failure of ART
- I do not order SDF testing for RPL
- Not applicable

**17. In which of the following conditions, risk factors, or exposures would you order SDF testing for infertile men (in actual practice)? [Select all that apply]**

- Age >40 years
- Smoking (>10 cigarettes per day)
- Heavy alcohol intake
- Diabetes
- Obesity (BMI >30 kg/m<sup>2</sup>)
- Sedentary lifestyle
- Male genital tract infection/inflammation
- >1 million/ml round cells on semen analysis
- Necrozoospermia on semen analysis
- Spinal cord injury
- Male genital tract trauma/surgery
- History of testicular cancer
- History of chemotherapy
- History of radiotherapy to pelvic area
- Recreational drug use
- Environmental pollution exposure
- Chemical exposure
- Radiation exposure
- Heat exposure
- Very low frequency of ejaculations (<3 per month)
- I do not order SDF testing for any of these conditions
- Not applicable

**18. In an infertile patient with clinical varicocele and abnormal conventional semen parameters, when do you order SDF testing? [Select all that apply]**

- At initial evaluation in all patients
- After failure of conservative management (such as: antioxidants, medical therapy)
- Before varicocele repair
- Persistent infertility despite varicocele repair
- Before referral for ART
- After failure of ART
- I do not order SDF testing for men with clinical varicocele and abnormal semen parameters
- Not applicable

**19. In an infertile patient with clinical varicocele and normal conventional semen parameters, do you order SDF testing?**

- Yes, at initial evaluation in all patients
- Yes, to justify surgery in patients who may be candidates for repair
- Yes, only if ART is planned
- No, I do not order SDF testing for men with clinical varicocele and normal semen parameters
- Not applicable

20. **In an infertile patient with subclinical varicocele and abnormal conventional semen parameters, do you order SDF testing?**

- Yes, at initial evaluation in all patients
- Yes, only after failure of medical management
- Yes, only if ART is planned
- No, I do not order SDF testing for men with subclinical varicocele and abnormal conventional semen parameters
- Not applicable

21. **In an infertile patient with subclinical varicocele and normal conventional semen parameters, do you order SDF testing?**

- Yes, at initial evaluation in all patients
- Yes, only after failure of medical management
- Yes, only if ART is planned
- No, I do not order SDF testing for men with subclinical varicocele and normal conventional semen parameters
- Not applicable

22. **Do you perform SDF testing for infertile men of couples who are undergoing ART?**

- Yes, always
- Yes, only for certain indications
- No, I do not order SDF testing before ART
- Not applicable

23. **In couples undergoing ART, which of the following infertile men would you test for SDF? [Select all that apply]**

- UMI
- IMI
- Recurrent natural pregnancy loss
- Clinical varicocele (untreated)
- Clinical varicocele (treated)
- Subclinical varicocele
- Male age >40 years
- Risk factors and exposures
- I do not order SDF testing before ART
- Not applicable

24. **When would you consider SDF testing for men of partners undergoing IUI? [Select all that apply]**

- Starting IUI
- First failure of IUI (inability to achieve clinical pregnancy)
- Recurrent IUI failure
- First miscarriage after IUI
- Recurrent miscarriage after IUI
- I do not order SDF testing before IUI
- Not applicable

25. **When would you consider SDF testing for men of partners undergoing IVF? [Select all that apply]**

- Before IVF
- First IVF failure due to failed fertilization
- First IVF failure due to failed implantation

- First IVF failure due to early pregnancy loss
- Recurrent fertilization failure after IVF
- Recurrent implantation failure after IVF
- Recurrent pregnancy loss after IVF
- I do not order SDF testing before IVF
- Not applicable

26. **When would you consider SDF testing for men of partners undergoing ICSI? [Select all that apply]**

- Before ICSI
- First ICSI failure due to failed fertilization
- First ICSI failure due to failed implantation
- First ICSI failure due to early pregnancy loss
- Recurrent fertilization failure after ICSI
- Recurrent implantation failure after ICSI
- Recurrent pregnancy loss after ICSI
- I do not order SDF testing before ICSI
- Not applicable

27. **Do you order SDF testing before sperm cryopreservation?**

- Yes, for all patients
- Yes, only if there are abnormalities on conventional semen analysis
- Yes, only if there are underlying conditions and risk factors
- No, I do not order SDF testing for cryopreservation.
- Not applicable

28. **If SDF testing is ordered before sperm cryopreservation, what implications would this have on your further approach? [Select all that apply]**

- Recommend against cryopreservation if SDF elevated
- Treat SDF before cryopreservation (if patient condition allows)
- Cryopreservation with additional antioxidants (ex-vivo)
- Refer directly to ICSI after thawing
- No implication, just provide additional information to counsel patients
- I do not order SDF testing for cryopreservation
- Not applicable

## **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

### **SECTION III: Technical aspects of SDF testing**

Abbreviations: SDF: sperm DNA fragmentation; ART: assisted reproductive technology; IUI: intrauterine insemination; IVF: in-vitro fertilization; ICSI: intracytoplasmic sperm injection; UMI: unexplained male infertility; IMI: idiopathic male infertility; RPL: recurrent pregnancy loss.

Instructions to participants: Please answer all questions. The option "Not Applicable" is available if you do not encounter such a case in your practice.

29. **Which of the following SDF assays do you order? (If you use more than one, choose the most commonly ordered test in your practice)**

- Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL)
- Sperm chromatin dispersion (SCD)
- Sperm chromatin structure assay (SCSA)
- Comet
- Other test
- Not applicable

30. **Which of the following factors determine your choice of the assay? [Select all that apply]**

- Availability
- Cost of performing
- Additional cost for patient
- Ease of performing by biologists
- Short time needed to obtain result
- Ease of interpretation
- Accuracy
- Training of staff and personnel
- Evidence provided in literature on each assay
- Not applicable

31. **Which of the following thresholds do you use to interpret the test results?**

- 20% or higher is elevated SDF
- 25% or higher is elevated SDF
- 30% or higher is elevated SDF
- Threshold determined by my lab
- Threshold provided by testing lab
- Other
- Not applicable

32. **Do you recommend an abstinence period before SDF testing (including last discarded ejaculation if applicable)?**

- No
- Yes, less than 24 hours
- Yes, 24-48 hours
- Yes, 3-5 days
- Yes, 6 days or more
- Not applicable

**Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**



#### **SECTION IV: Treatment of elevated SDF**

Abbreviations: SDF: sperm DNA fragmentation; ART: assisted reproductive technology; IUI: intrauterine insemination; IVF: in-vitro fertilization; ICSI: intracytoplasmic sperm injection; UMI: unexplained male infertility; IMI: idiopathic male infertility; RPL: recurrent pregnancy loss.

Instructions to participants: Please answer all questions. The option "Not Applicable" is available if you do not encounter such a case in your practice.

33. **How do you treat elevated SDF once diagnosed in infertile men? [Select all that apply]**
- Repeat testing and confirm elevated SDF
  - Recommend lifestyle changes (smoking cessation, weight loss, etc.)
  - Recommend reduced ejaculatory abstinence
  - Prescribe empiric antioxidants
  - Prescribe empiric antibiotics (without culture)
  - Prescribe empiric hormonal therapy
  - Refer directly for ART with ejaculated sperm
  - Refer directly for ART with advanced sperm selection techniques
  - Refer directly for ICSI with testicular sperm
  - Not applicable
34. **What duration of abstinence do you recommend for infertile men with elevated SDF before attempting conception (whether natural or by ART)?**
- Less than 24 hours
  - 24-48 hours
  - 3-5 days
  - 6 days or more
  - I do not recommend reduced abstinence
  - Not applicable
35. **At which point would you refer a man with UMI and high SDF for ART, given there is no female factor infertility and the woman is under 35 years old?**
- Immediately after diagnosis
  - 3 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - More than 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - I do not refer men with UMI and elevated SDF for ART
  - Not applicable
36. **At which point would you refer a man with IMI and high SDF for ART, given there is no female factor infertility and the woman is under 35 years old?**
- Immediately after diagnosis
  - 3 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - More than 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
  - I do not refer men with IMI and elevated SDF for ART
  - Not applicable
37. **Which of the following would you recommend for a couple experiencing natural RPL, with a normal female partner and a male partner with high SDF, as an initial approach? [Select all that apply]**
- Reduced Abstinence
  - Lifestyle modification and avoiding environmental risks

- Empiric antioxidants
- Empiric hormonal therapy
- Empiric antibiotic therapy
- ART
- ICSI with testicular sperm
- Not applicable

38. **At which point would you refer a couple with natural RPL and high SDF in the man for ART, given there is no female factor infertility and the woman is under 35 years old?**

- Immediately after diagnosis
- 3 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- More than 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- I do not refer men with RPL and elevated SDF for ART
- Not applicable

39. **Which of the following would you recommend for a man with clinical varicocele, normal semen parameters, and high SDF, as an initial approach? [Select all that apply]**

- Varicocele repair (regardless of female factors)
- Varicocele repair (only if female partner is <38 years with good ovarian reserve)
- Reduced Abstinence
- Avoiding lifestyle and environmental risks
- Antioxidants
- Empiric hormonal therapy
- Directly proceed to ART (regardless of female factors)
- Directly proceed to ART (if female partner is >38 years)
- Not applicable

40. **At which point do you perform varicocele repair for a man with clinical varicocele, normal semen parameters, and elevated SDF?**

- Immediately after diagnosis
- 3 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- More than 6 months after failure of empiric medical therapy (e.g.: antioxidants) and conservative measures
- After failure of ART and no female factor
- I do not perform varicocele repair for men with clinical varicocele, normal semen parameters, and elevated SDF
- Not applicable

41. **At which point would you refer a man with clinical varicocele, normal semen parameters, and high SDF for ART, given there is no female factor infertility and the woman is under 35 years old?**

- Immediately after diagnosis
- After failure of varicocele repair
- After failure of conservative measures (without varicocele repair)
- I do not refer men with clinical varicocele, normal semen parameters, and elevated SDF for ART
- Not applicable

42. **During the evaluation of an infertile man, he is found to have elevated SDF as well as subclinical varicocele, would you offer varicocele repair for this patient?**

- Yes, in all such cases

- Yes, only if there are no other underlying causes and risks for elevated SDF
- Yes, only if ART is planned
- No, I do not repair subclinical varicocele
- Not applicable

**43. Do you prescribe antioxidants for infertile men with elevated SDF?**

- Yes, always
- Yes, depending on the associated underlying causes and risk factors
- No, I do not prescribe antioxidants for infertile men with elevated SDF
- Not applicable

**44. For which of the following conditions associated with elevated SDF do you prescribe antioxidants as a primary line of therapy? [Select all that apply]**

- Aging
- Smoking
- Obesity
- Exposures (occupational, environmental)
- UMI
- IMI
- RPL, no other causes found
- Clinical varicocele
- Subclinical varicocele
- Male genital tract infections
- Leukocytospermia
- Spinal cord injury
- ART failure
- None
- Not applicable

**45. Which of the following antioxidants (either as single agents or as a combination) do you prescribe for infertile with elevated SDF? [Select all that apply]**

- Zinc
- Selenium
- L-carnitine
- Acetyl carnitine
- Lycopene
- L-arginine
- Glutathione
- N-acetyl cysteine
- Co-enzyme Q10
- Docosahexanoic acid (DHA)
- Melatonin
- Vitamin A
- Vitamin C
- Vitamin E
- Folic Acid (B9)
- Other B vitamins
- Vitamin D
- Herbal products
- Other
- Not applicable

**46. What duration of treatment with antioxidants do you recommend for infertile men with elevated SDF?**

- Less than 3 months
- 3 months
- 4-6 months
- 7-12 months
- Until clinical pregnancy is achieved
- Not applicable

**47. How do you follow up on treatment success after antioxidant supplementation in infertile men with elevated SDF?**

- Demonstration of reduced SDF on repeat testing
- Clinical pregnancy
- Live birth
- I do not follow-up
- Not applicable

**48. Do you prescribe hormones for infertile men with elevated SDF?**

- Yes, always
- Yes, depending on the associated underlying causes and risk factors
- No, I do not prescribe hormones for infertile men with elevated SDF
- Not applicable

**49. Which hormones do you prescribe for infertile men with elevated SDF? [Select all that apply]**

- Follicle stimulating hormone (FSH)
- Human chorionic gonadotropin (hCG)
- Gonadotropin releasing hormone (GnRH)
- Aromatase inhibitors, such as letrozole, anastrozole, testolactone
- Selective estrogen receptor modulators (SERM), such as clomiphene citrate, tamoxifen
- Other
- Not applicable

**50. What duration of treatment with hormones do you recommend for infertile men with elevated SDF?**

- Less than 3 months
- 3 months
- 4-6 months
- 7-12 months
- Until clinical pregnancy is achieved
- Not applicable

**51. In a couple with a normal female partner experiencing failure to achieve a clinical pregnancy after IUI, associated with elevated SDF in the male partner, what would your management strategy be?**

- Repeat the procedure with no additional intervention
- Repeat the procedure after applying conservative measures (shorter abstinence, antioxidants)
- Repeat IUI using techniques to select sperm with lower SDF
- Refer for ICSI with ejaculated sperm

- Refer for ICSI using techniques to select sperm with lower SDF
  - Refer for ICSI using testicular sperm
  - Not applicable
52. **In a couple with a normal female partner experiencing miscarriage after IUI, associated with elevated SDF in the male partner, what would your management strategy be?**
- Repeat the procedure with no additional intervention
  - Repeat the procedure after applying conservative measures (shorter abstinence, antioxidants)
  - Repeat IUI using techniques to select sperm with lower SDF
  - Refer for ICSI with ejaculated sperm
  - Refer for ICSI using techniques to select sperm with lower SDF
  - Refer for ICSI using testicular sperm
  - Not applicable
53. **In a couple with a normal female partner experiencing fertilization failure after IVF, associated with elevated SDF in the male partner, what would your management strategy be?**
- Repeat the procedure with no additional intervention
  - Repeat the procedure after applying conservative measures (shorter abstinence, antioxidants)
  - Repeat IVF using techniques to select sperm with lower SDF
  - Refer for ICSI with ejaculated sperm
  - Refer for ICSI using techniques to select sperm with lower SDF
  - Refer for ICSI using testicular sperm
  - Not applicable
54. **In a couple with a normal female partner experiencing failure to achieve a clinical pregnancy after IVF, associated with elevated SDF in the male partner, what would your management strategy be?**
- Repeat the procedure with no additional intervention
  - Repeat the procedure after applying conservative measures (shorter abstinence, antioxidants)
  - Repeat IVF using techniques to select sperm with lower SDF
  - Refer for ICSI with ejaculated sperm
  - Refer for ICSI using techniques to select sperm with lower SDF
  - Refer for ICSI using testicular sperm
  - Not applicable
55. **In a couple with a normal female partner experiencing miscarriage after IVF or ICSI, associated with elevated SDF in the male partner and no other abnormality, what would your management strategy be?**
- Repeat the procedure with no additional intervention
  - Repeat the procedure after applying conservative measures (shorter abstinence, antioxidants)
  - Repeat IVF or ICSI using techniques to select sperm with lower SDF
  - Refer for ICSI using testicular sperm
  - Transfer to another center
  - Not applicable
56. **Do you recommend sperm selection techniques for infertile men with elevated SDF?**
- Yes, always if the couple is planned for ART with male partner having high SDF
  - Yes, only for repeat ART after initial failure with male partner having high SDF
  - No, I do not recommend sperm selection techniques

**57. Which sperm selection techniques do you use or recommend for men with elevated SDF?**

**[Select all that apply]**

- Density gradient centrifugation (DGC)
- Magnetic-activated cell sorting (MACS)
- Intracytoplasmic morphologically selected sperm injection (IMSI)
- Physiological intracytoplasmic sperm injection (P-ICSI)
- Microfluidics
- Other
- Not applicable

**58. Do you recommend the use of testicular sperm for men with elevated SDF undergoing ICSI?**

- Yes, routinely
- Yes, only in some cases
- No, I do not recommend testicular sperm for infertile men with elevated SDF
- Not applicable

**59. If you answered yes, when would you recommend testicular sperm for ICSI for men with elevated SDF?**

- At first planned ICSI
- After failure of one ICSI cycle
- After two or more ICSI failures with sperm selection
- I do not recommend testicular sperm extraction for men with elevated SDF
- Not applicable

**60. If you answered no, why do you not recommend testicular sperm for men with elevated SDF?**

**[Select all that apply]**

- Invasive procedure
- Possible surgical complications
- Risk of formation of antisperm antibodies
- Inadequate evidence to support such a decision
- Expensive
- Not applicable

## **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

### **SECTION V: Barriers and limitations in incorporating SDF testing into clinical practice**

Abbreviations: SDF: sperm DNA fragmentation; ART: assisted reproductive technology; IUI: intrauterine insemination; IVF: in-vitro fertilization; ICSI: intracytoplasmic sperm injection; UMI: unexplained male infertility; IMI: idiopathic male infertility; RPL: recurrent pregnancy loss.

Instructions to participants: Please answer all questions. The option "Not Applicable" is available if you do not encounter such a case in your practice.

**61. Which of the following factors limit YOUR ABILITY to order SDF testing? [Select all that**

**apply]\***

- Unavailability of assays
- Cost of testing
- Not covered by insurance
- Lack of clear recommendations for testing
- Lack of information on SDF testing
- Lack of standardized SDF measurement technique
- No agreed reference and cut-off values
- Concern about interpretation of results
- Patients not convinced of additional tests
- I am not convinced of SDF testing
- I have no limitations in ordering SDF testing
- Not applicable

**62. Assuming all resources are available, do you BELIEVE (regardless of your actual practice) SDF should be ordered in the evaluation of infertile men? [Select all that apply]\***

- Yes, for all infertile men
- Yes, for all men with UMI
- Yes, for all men with IMI
- Yes, for all men with causes and risks known to elevate SDF
- Yes, before referral for ART in all cases of male infertility
- Yes, after failure of ART for all cases
- Yes, after first natural pregnancy loss
- Yes, after natural RPL
- Yes, for surgery decision on subclinical varicocele
- Yes, for surgery decision on clinical varicocele with normal semen parameters
- No, SDF testing should occur only for select few patients after careful evaluation
- No, SDF testing should have no role in evaluation of male infertility
- Not applicable

**63. In your opinion, why is there a delay in incorporating SDF testing into clinical practice? [Select all that apply]\***

- No clear recommendations by society guidelines
- No reliable results and large variability between labs
- No globally accepted reference ranges
- Poor quality research available regarding the topic
- Unavailable SDF testing
- Difficulty in performing SDF testing
- Resistance by many clinicians to incorporate this new technology into their practice
- Too expensive in time and/or material to be used routinely
- Insurance companies will not cover costs of testing
- Economic drawbacks of SDF testing outweigh the benefits that may be conferred to patients
- For large number of SDF tests conducted, only a small proportion of patients will benefit
- Knowing whether SDF is high or low will typically not affect the management plan
- Not applicable

**64. In your opinion and based on your experience, why should SDF testing be incorporated more into clinical practice? [Select all that apply]\***

- Provide an explanation to many unknown causes of male infertility
- Provide basis for counselling patients, especially regarding lifestyle risks
- Availability of commercial assays that are relatively affordable and easy to interpret

- Avoid unnecessary cost, time, and resources of ART
- Allow targeted treatment approaches and personalized medicine
- I do not believe it should be incorporated more into clinical practice
- Not applicable

## **Controversy and Consensus in the Use of Sperm DNA Fragmentation Test in the Management of Male Infertility: Results of a Global Survey of Reproductive Clinicians and comparison with Professional Society Guidelines and Expert Recommendations.**

Dear Participant,

Thank you for taking the time to complete our survey.

In order to increase our outreach and to be able to capture a broader viewpoint on the current practices regarding SDF testing and management, we are asking you to provide the names and email addresses of five or more experts who are directly involved in the management of infertile couples. We will invite them to fill out this survey. We very much appreciate your help.

Thank you.

65. **Expert 1 name:**

66. **Expert 1 email address:**

67. **Expert 2 name:**

68. **Expert 2 email address:**

69. **Expert 3 name:**

70. **Expert 3 email address:**

71. **Expert 4 name:**

72. **Expert 4 email address:**



73. **Expert 5 name:**

74. **Expert 5 email address:**

75. **Expert 6 name:**

76. **Expert 6 email address:**

77. **Expert 7 name:**

78. **Expert 7 email address:**

79. **Expert 8 name:**

80. **Expert 8 email address:**

81. **Expert 9 name:**

82. **Expert 9 email address:**

83. **Expert 10 name:**

84. **Expert 10 email address:**